US007435221B1

(12) **United States Patent**
Bharmi et al.

(10) **Patent No.: US 7,435,221 B1**
(45) **Date of Patent: Oct. 14, 2008**

(54) **SYSTEM AND METHOD FOR DETECTING ABNORMAL RESPIRATION BASED ON INTRACARDIAC ELECTROGRAM SIGNALS USING A PATTERN RECOGNITION DEVICE**

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(73) Assignee: **Pacesetter, Inc.**, Sylmar, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 83 days.

(21) Appl. No.: **11/558,819**

(22) Filed: **Nov. 10, 2006**

Related U.S. Application Data

(63) Continuation-in-part of application No. 11/416,317, filed on May 1, 2006, now Pat. No. 7,361,146, which is a continuation-in-part of application No. 11/127,389, filed on May 11, 2005.

(60) Provisional application No. 60/631,111, filed on Nov. 24, 2004.

(51) **Int. Cl.**
A61B 5/08 (2006.01)
A61B 5/02 (2006.01)
A61B 5/04 (2006.01)

(52) **U.S. Cl.** **600/484**; 600/529; 600/513; 600/509

(58) **Field of Classification Search** 600/481, 600/483, 484, 500–503, 508–529; 607/2–32
See application file for complete search history.

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Primary Examiner—Charles A. Marmor, II
Assistant Examiner—Navin Natnithithadha

(57) **ABSTRACT**

Techniques are provided for detecting abnormal respiration within a patient based upon intracardiac electrogram (IEGM) signals or other electrical cardiac signals. Briefly, abnormal respiration is detected using a pattern recognition trained to discriminate normal and abnormal respiration based on morphological parameters and interval-based parameters extracted from the IEGM signals. In addition, techniques are described for distinguishing among different cardiac rhythm types within the patient while using one or more pattern classifiers or other pattern recognition devices.

16 Claims, 34 Drawing Sheets

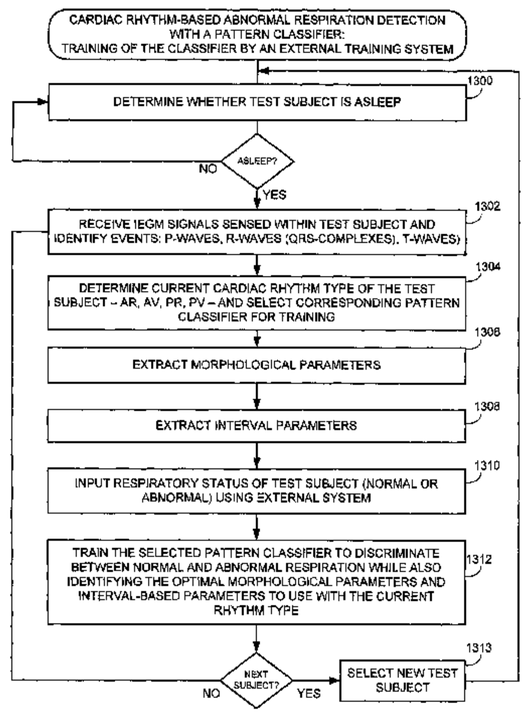

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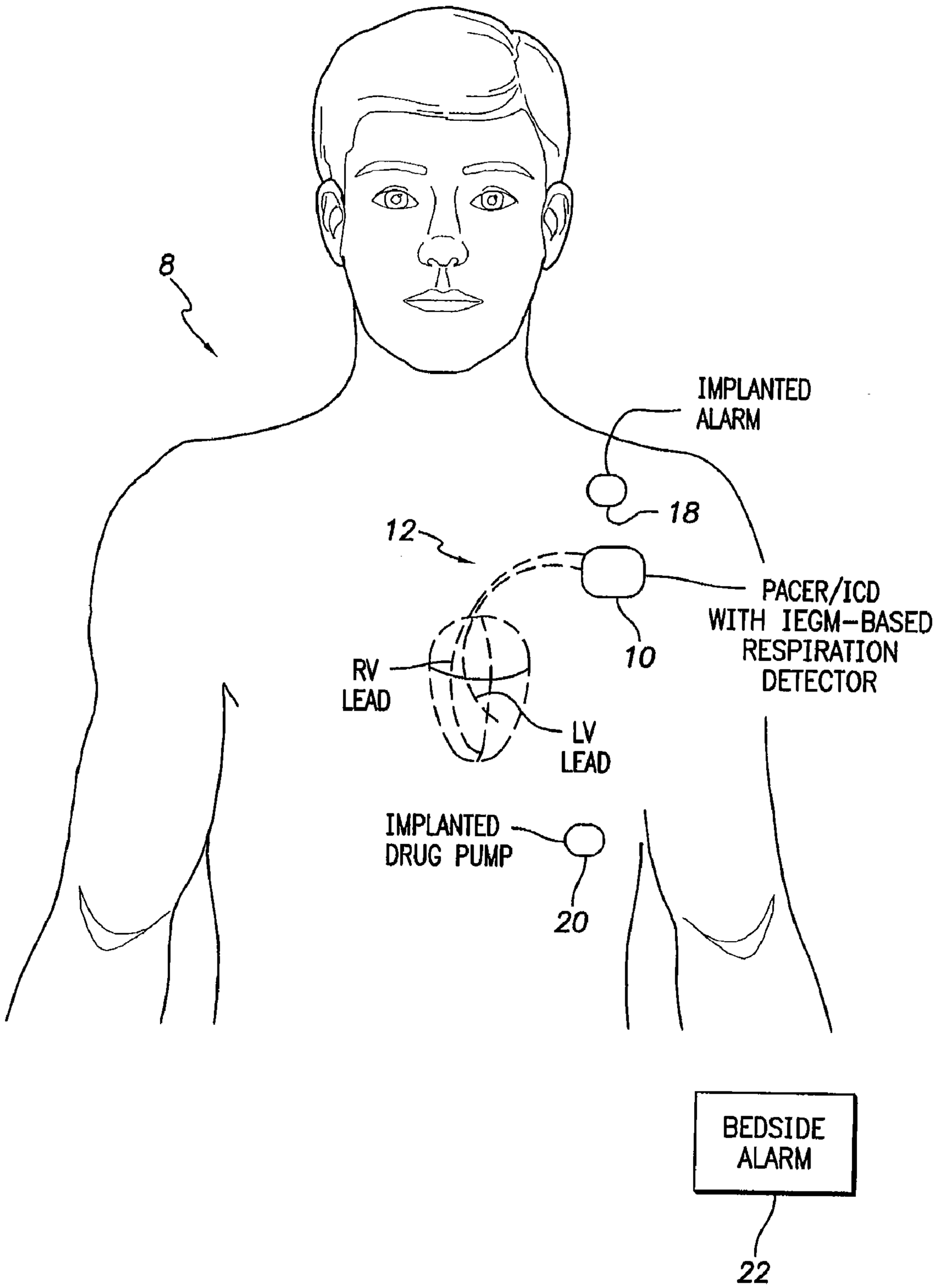
FIG. 1


8
IMPLANTED ALARM
18
12
PACER/ICD WITH IEGM-BASED RESPIRATION DETECTOR
10
RV LEAD
LV LEAD
IMPLANTED DRUG PUMP
20
BEDSIDE ALARM
22

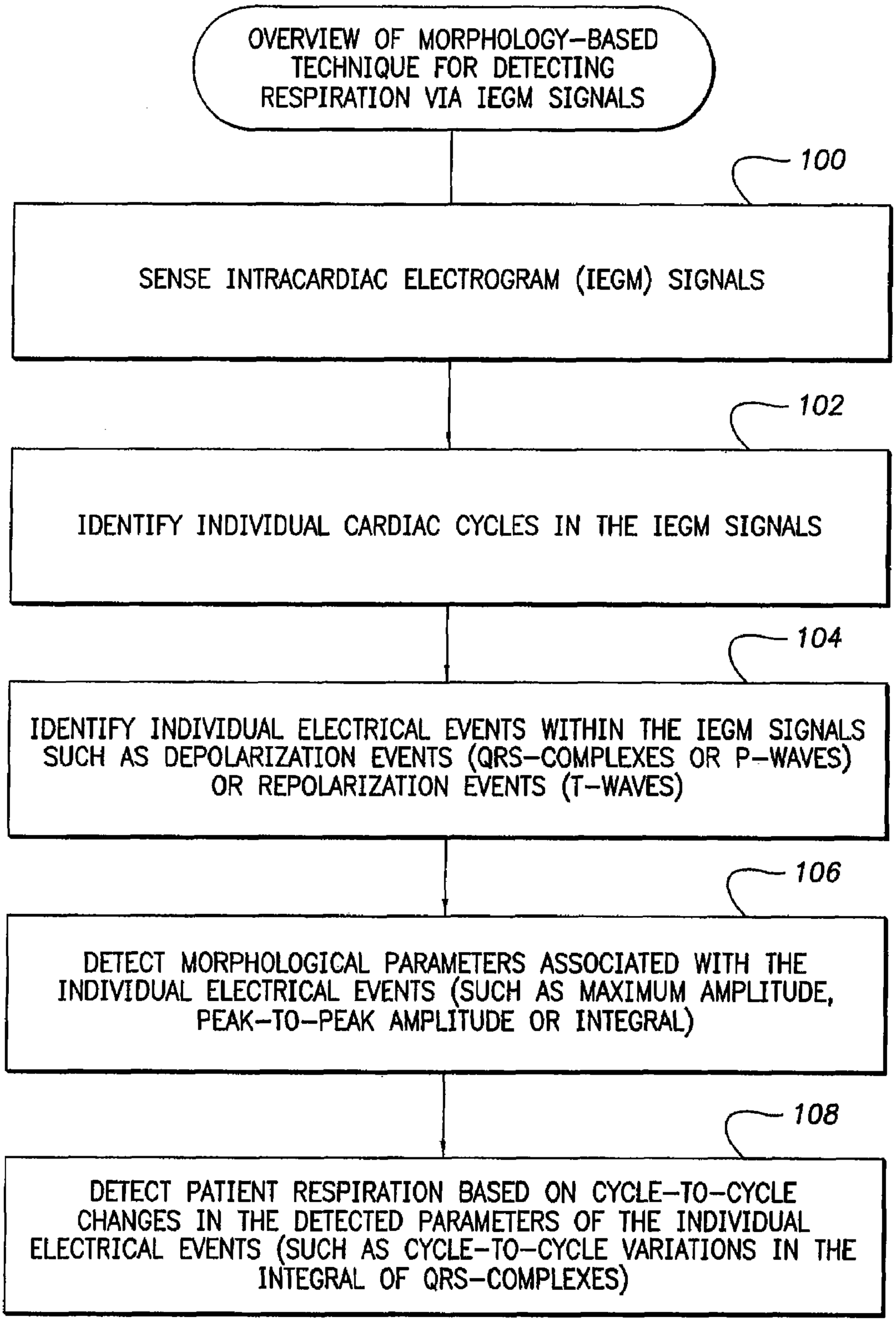

OVERVIEW OF MORPHOLOGY-BASED TECHNIQUE FOR DETECTING RESPIRATION VIA IEGM SIGNALS
100
SENSE INTRACARDIAC ELECTROGRAM (IEGM) SIGNALS
102
IDENTIFY INDIVIDUAL CARDIAC CYCLES IN THE IEGM SIGNALS
104
IDENTIFY INDIVIDUAL ELECTRICAL EVENTS WITHIN THE IEGM SIGNALS SUCH AS DEPOLARIZATION EVENTS (QRS-COMPLEXES OR P-WAVES) OR REPOLARIZATION EVENTS (T-WAVES)
106
DETECT MORPHOLOGICAL PARAMETERS ASSOCIATED WITH THE INDIVIDUAL ELECTRICAL EVENTS (SUCH AS MAXIMUM AMPLITUDE, PEAK-TO-PEAK AMPLITUDE OR INTEGRAL)
108
DETECT PATIENT RESPIRATION BASED ON CYCLE-TO-CYCLE CHANGES IN THE DETECTED PARAMETERS OF THE INDIVIDUAL ELECTRICAL EVENTS (SUCH AS CYCLE-TO-CYCLE VARIATIONS IN THE INTEGRAL OF QRS-COMPLEXES)

FIG. 2

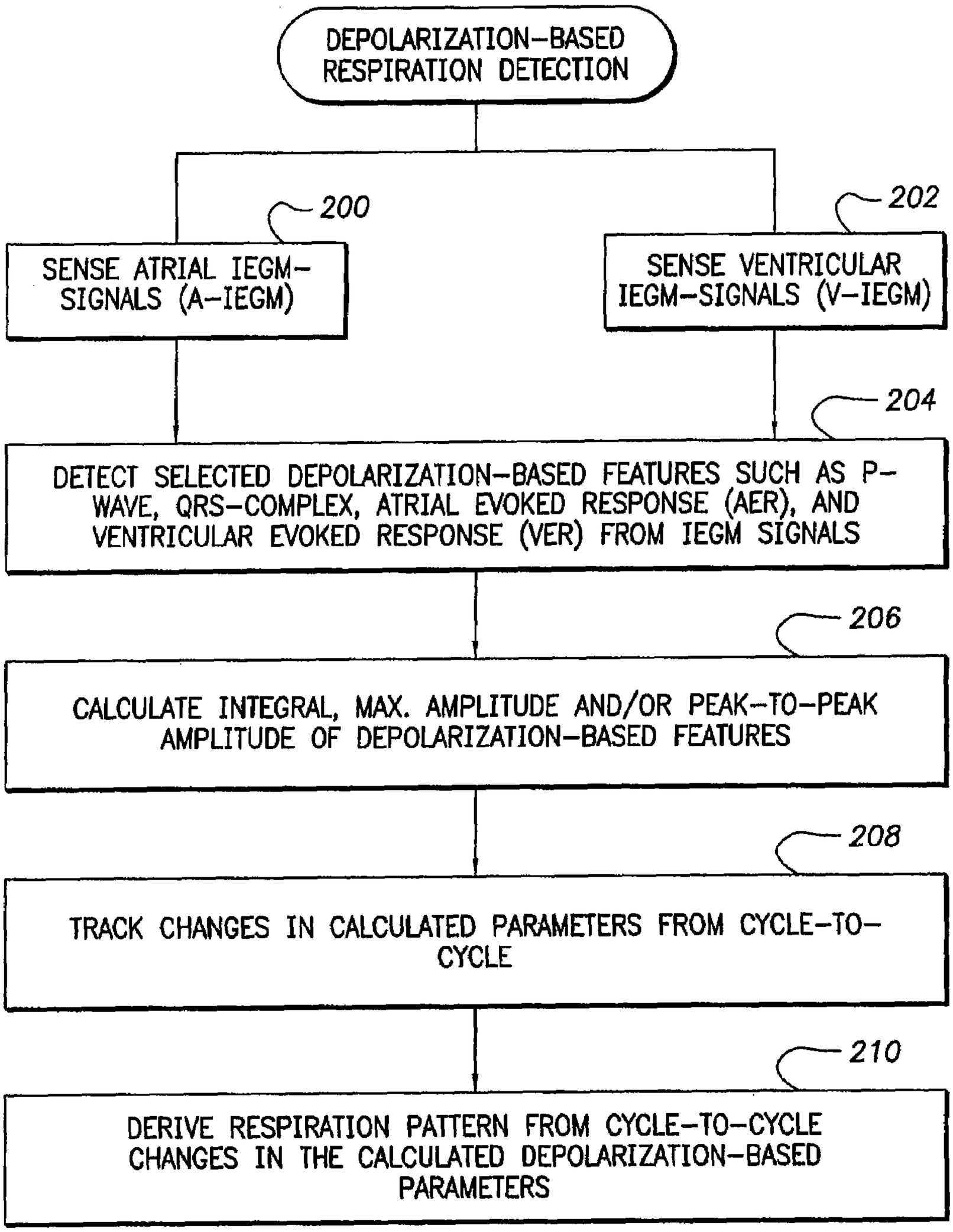

DEPOLARIZATION-BASED RESPIRATION DETECTION
200
SENSE ATRIAL IEGM-SIGNALS (A-IEGM)
202
SENSE VENTRICULAR IEGM-SIGNALS (V-IEGM)
204
DETECT SELECTED DEPOLARIZATION-BASED FEATURES SUCH AS P-WAVE, QRS-COMPLEX, ATRIAL EVOKED RESPONSE (AER), AND VENTRICULAR EVOKED RESPONSE (VER) FROM IEGM SIGNALS
206
CALCULATE INTEGRAL, MAX. AMPLITUDE AND/OR PEAK-TO-PEAK AMPLITUDE OF DEPOLARIZATION-BASED FEATURES
208
TRACK CHANGES IN CALCULATED PARAMETERS FROM CYCLE-TO-CYCLE
210
DERIVE RESPIRATION PATTERN FROM CYCLE-TO-CYCLE CHANGES IN THE CALCULATED DEPOLARIZATION-BASED PARAMETERS

FIG. 3

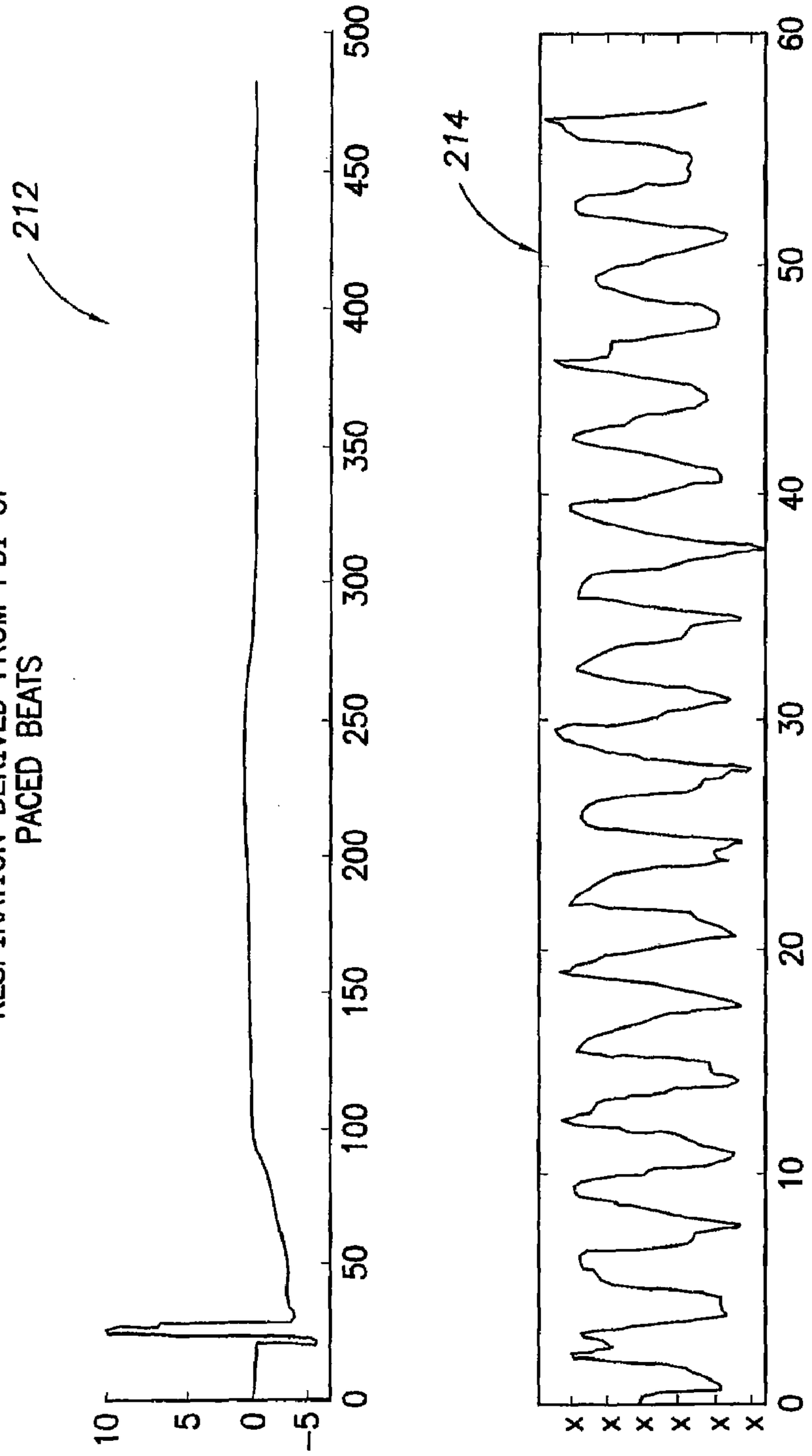

212
214
RESPIRATION DERIVED FROM PDI OF PACED BEATS
500
450
400
350
300
250
200
150
100
50
0
10
5
0
-5
60
50
40
30
20
10
0
SECONDS
PDI

FIG. 4

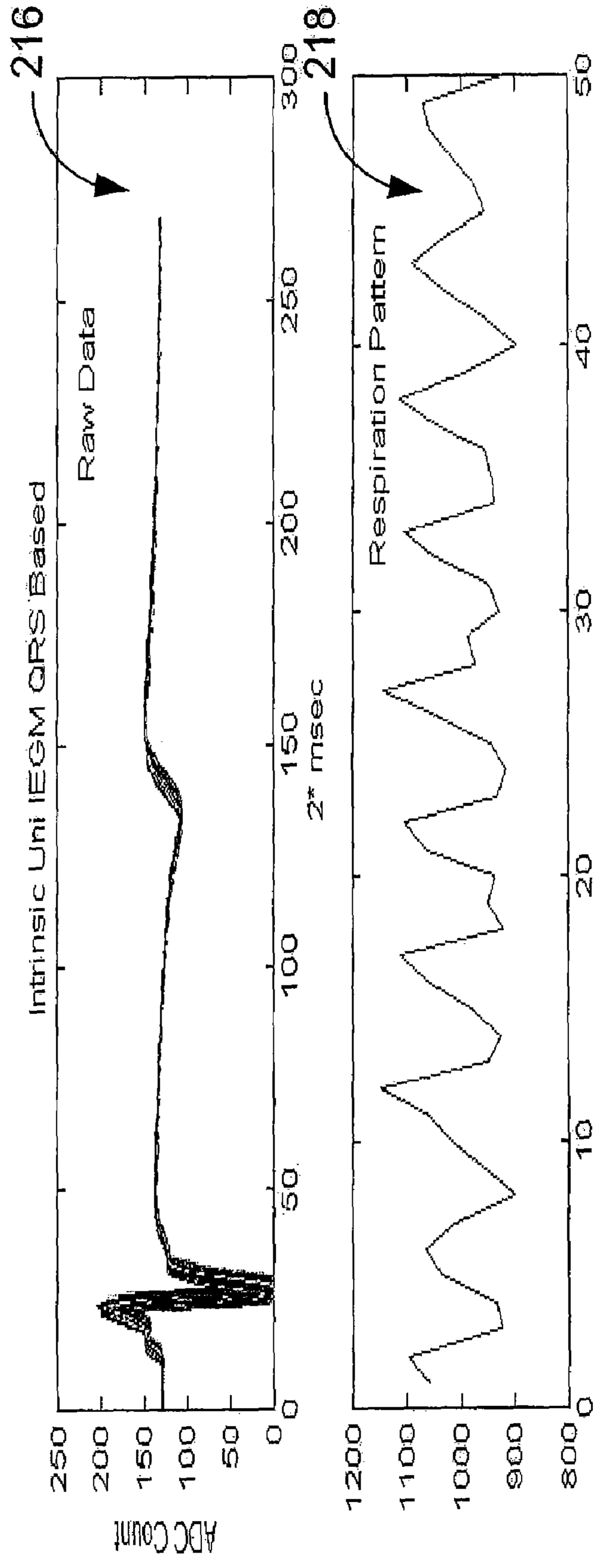

216
218
Intrinsic Uni IEGM QRS Based
Raw Data
ADC Count
250
200
150
100
50
0
300
250
200
150
100
50
2* msec
Respiration Pattern
50
40
30
20
10
0
1200
1100
1000
900
800
Beat number

FIG. 5

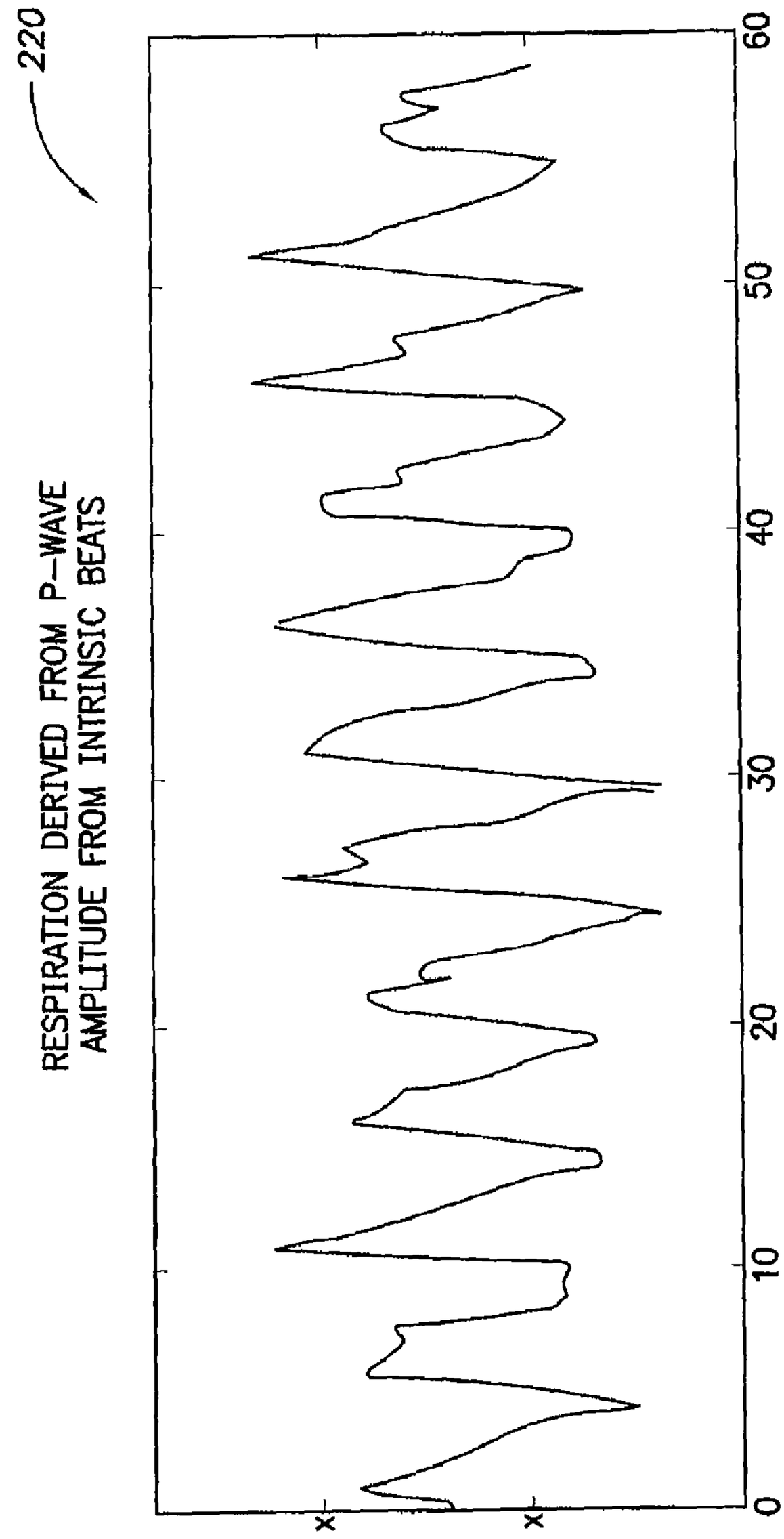

220
RESPIRATION DERIVED FROM P-WAVE AMPLITUDE FROM INTRINSIC BEATS
P-WAVE AMPLITUDE
SECONDS
0
10
20
30
40
50
60

FIG. 6

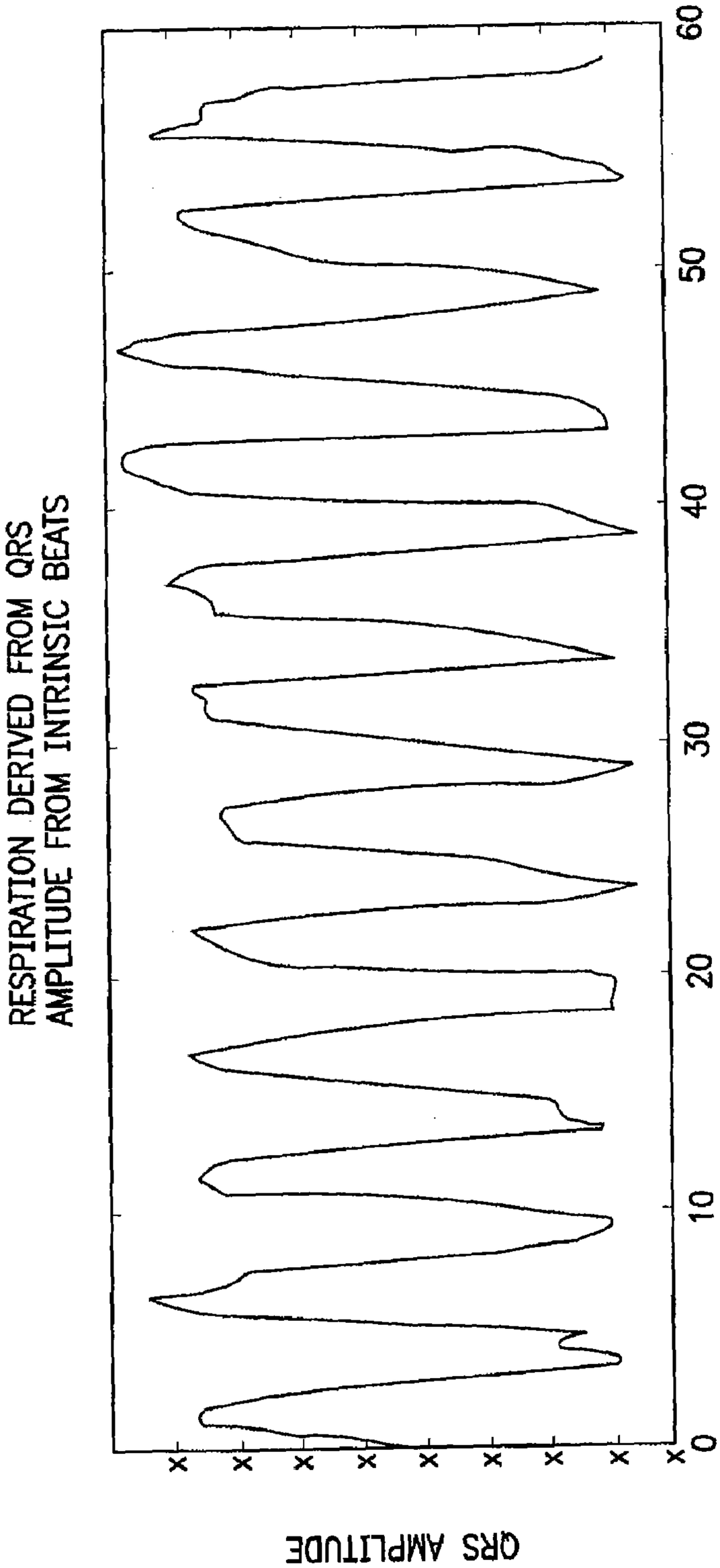

222
RESPIRATION DERIVED FROM QRS AMPLITUDE FROM INTRINSIC BEATS
QRS AMPLITUDE
0
10
20
30
40
50
60
SECONDS

FIG. 7

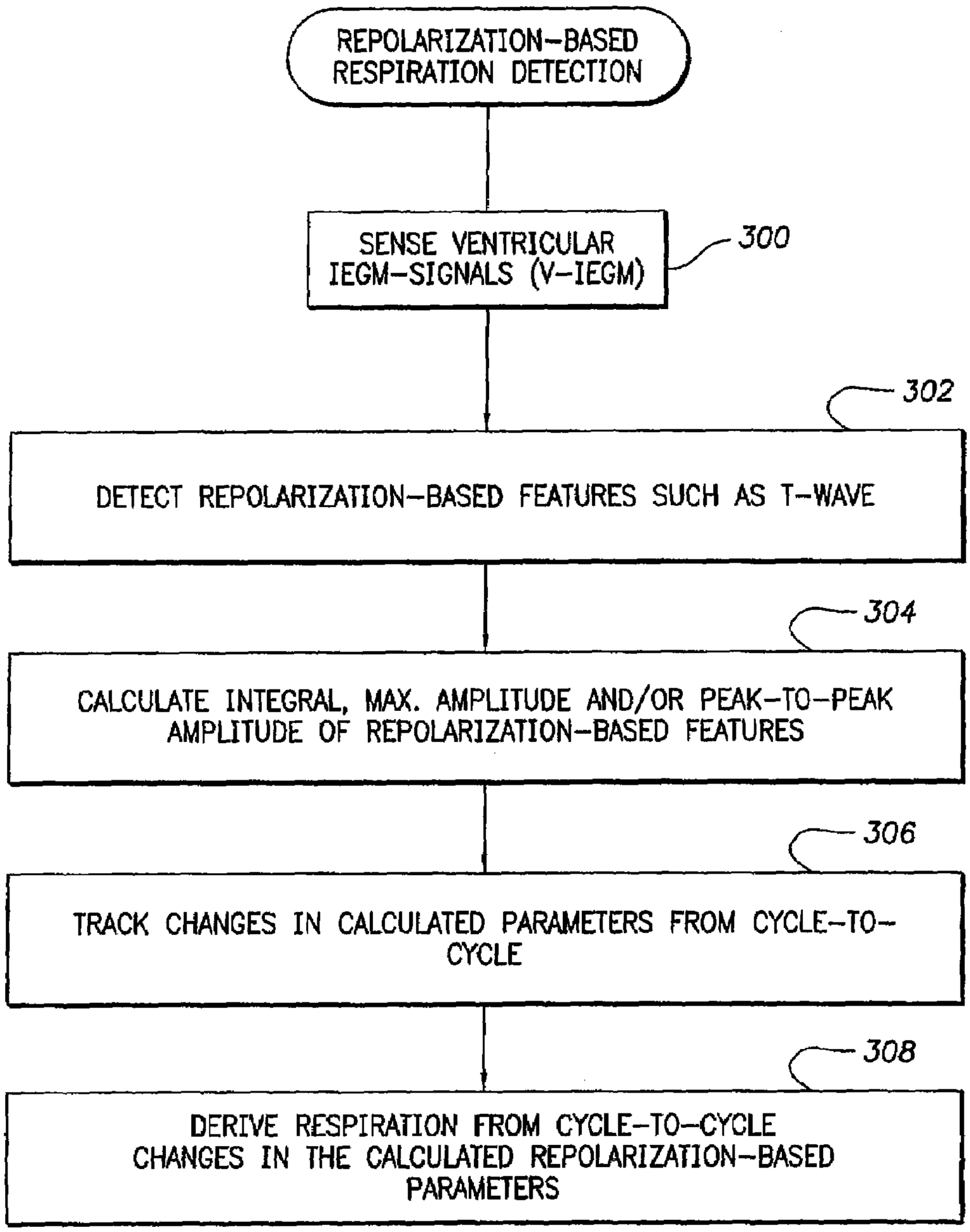

REPOLARIZATION-BASED RESPIRATION DETECTION
SENSE VENTRICULAR IEGM-SIGNALS (V-IEGM)
300
302
DETECT REPOLARIZATION-BASED FEATURES SUCH AS T-WAVE
304
CALCULATE INTEGRAL, MAX. AMPLITUDE AND/OR PEAK-TO-PEAK AMPLITUDE OF REPOLARIZATION-BASED FEATURES
306
TRACK CHANGES IN CALCULATED PARAMETERS FROM CYCLE-TO-CYCLE
308
DERIVE RESPIRATION FROM CYCLE-TO-CYCLE CHANGES IN THE CALCULATED REPOLARIZATION-BASED PARAMETERS

FIG. 8

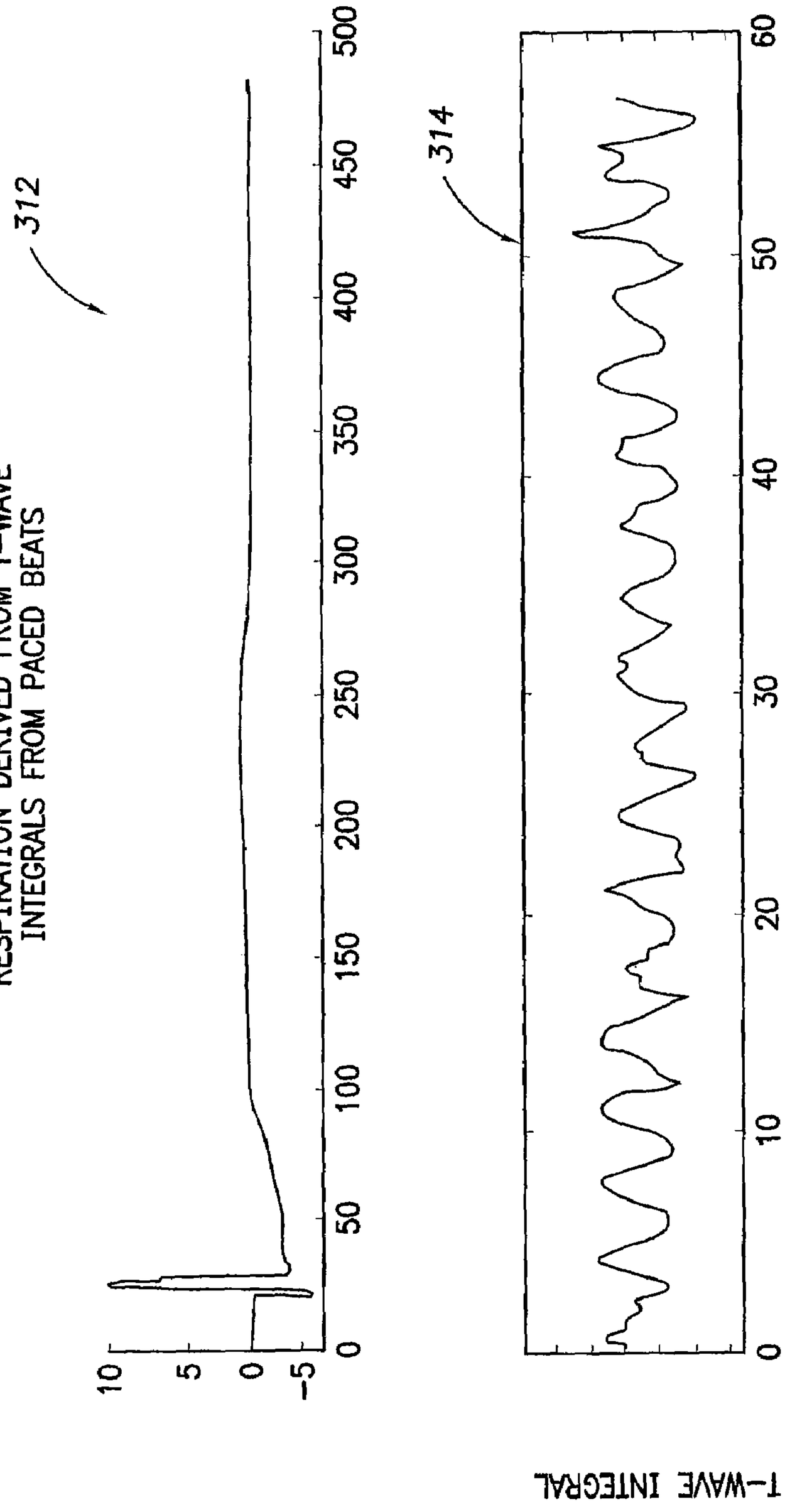

312
RESPIRATION DERIVED FROM T-WAVE INTEGRALS FROM PACED BEATS
500
450
400
350
300
250
200
150
100
50
0
10
5
0
-5
314
60
50
40
30
20
10
0
SECONDS
T-WAVE INTEGRAL

FIG. 9

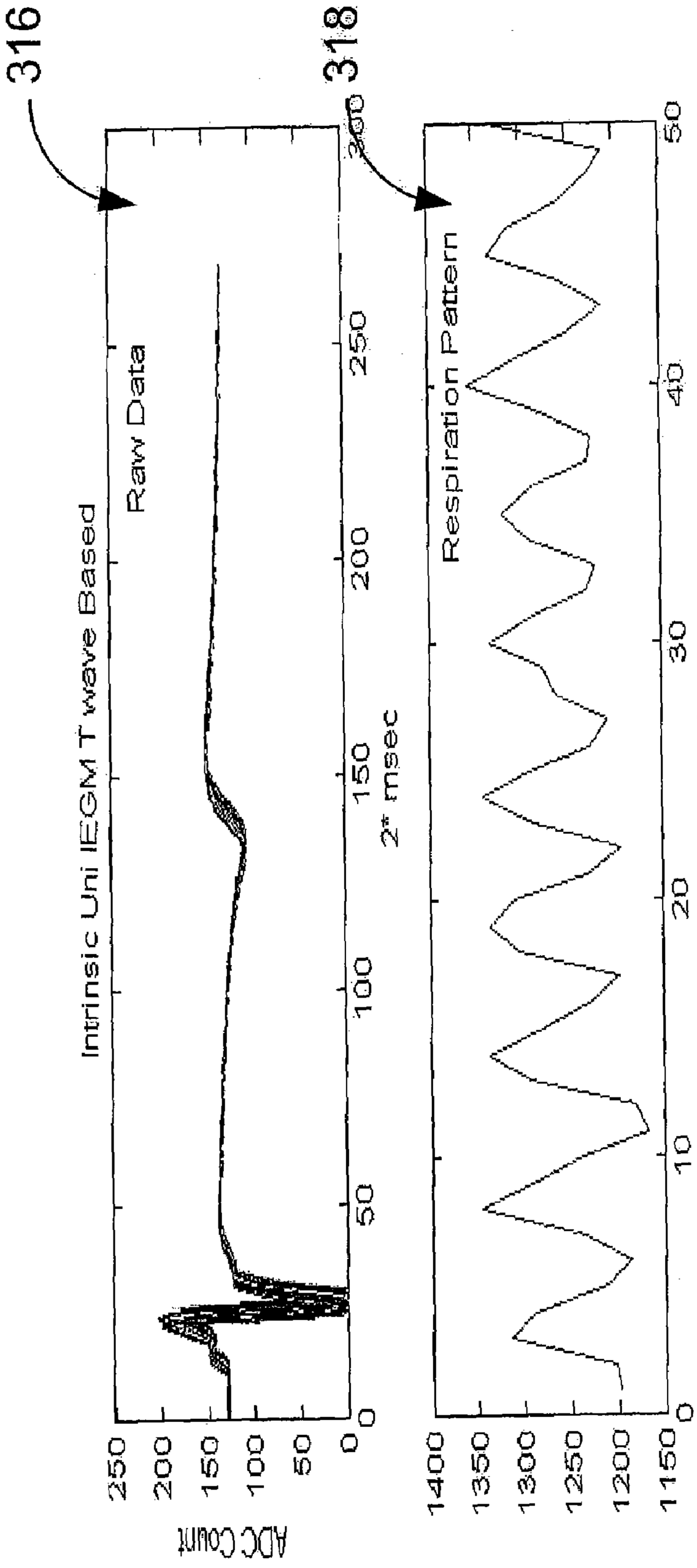

316
318
Intrinsic Uni IEGM T wave Based
Raw Data
ADC Count
2* msec
Respiration Pattern
Beat number

FIG. 10

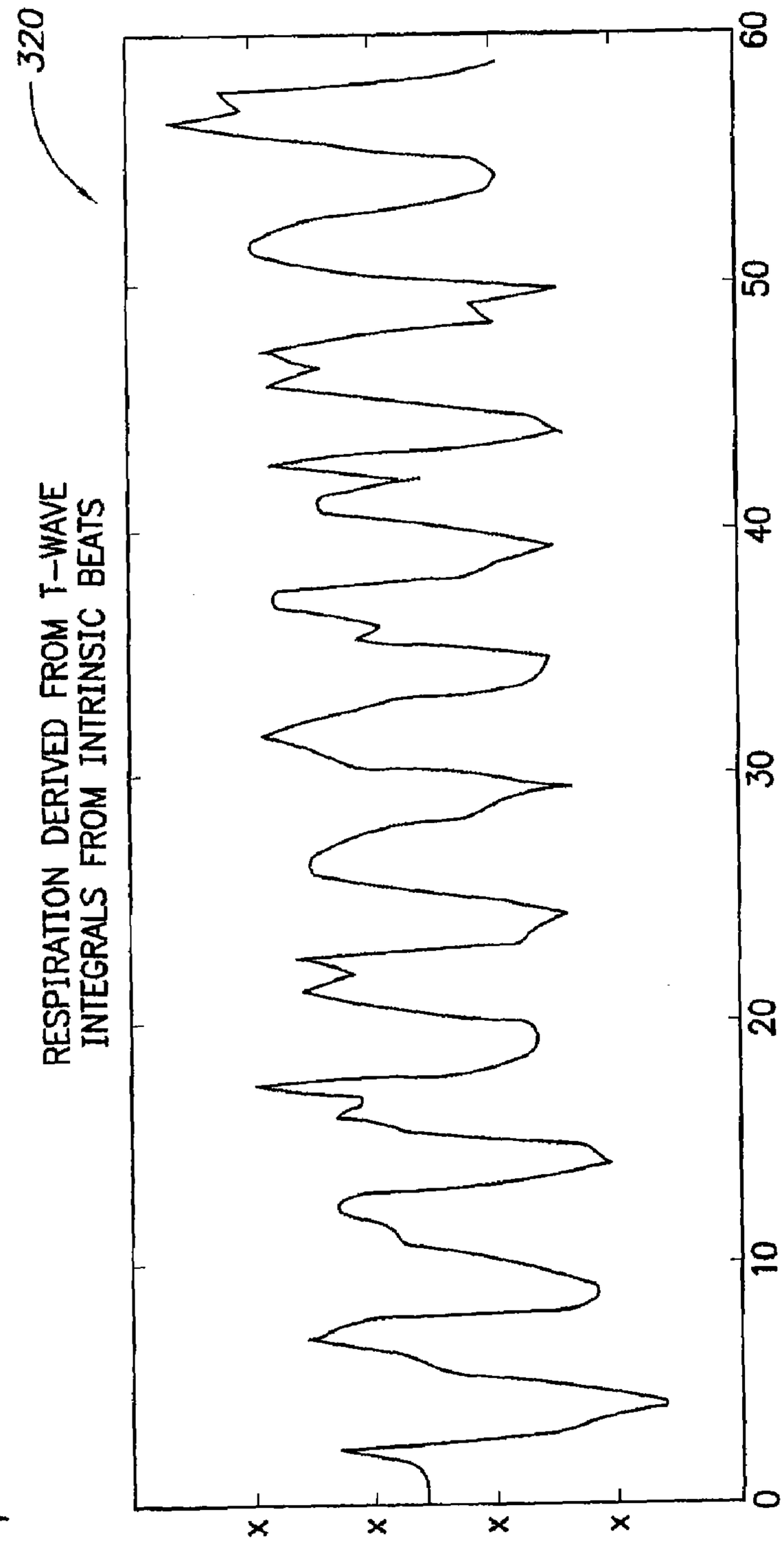

320
RESPIRATION DERIVED FROM T-WAVE
INTEGRALS FROM INTRINSIC BEATS
T-WAVE INTEGRAL
SECONDS
0
10
20
30
40
50
60

FIG. 11

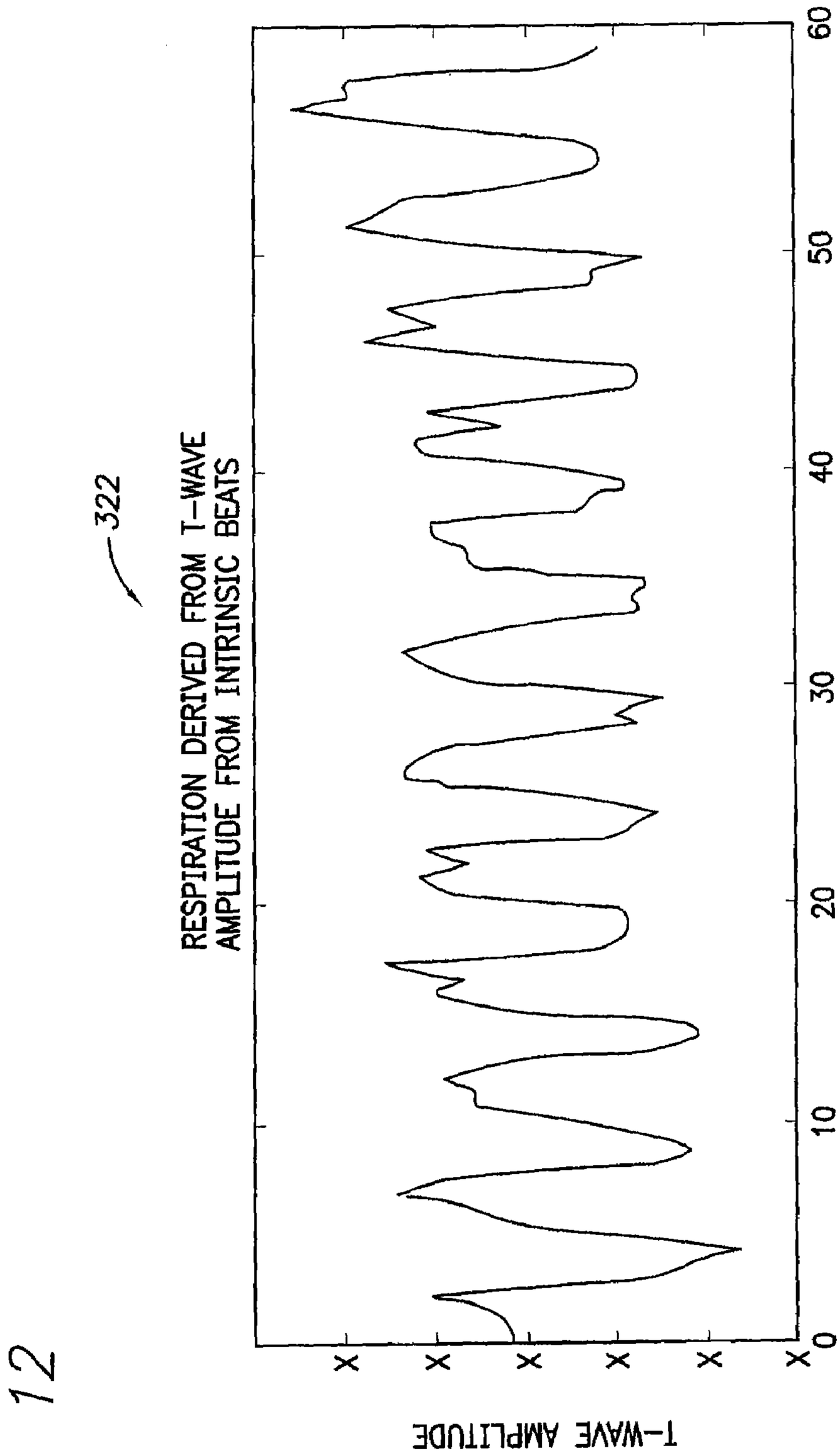

322
RESPIRATION DERIVED FROM T-WAVE AMPLITUDE FROM INTRINSIC BEATS
T-WAVE AMPLITUDE
SECONDS
0
10
20
30
40
50
60

FIG. 12

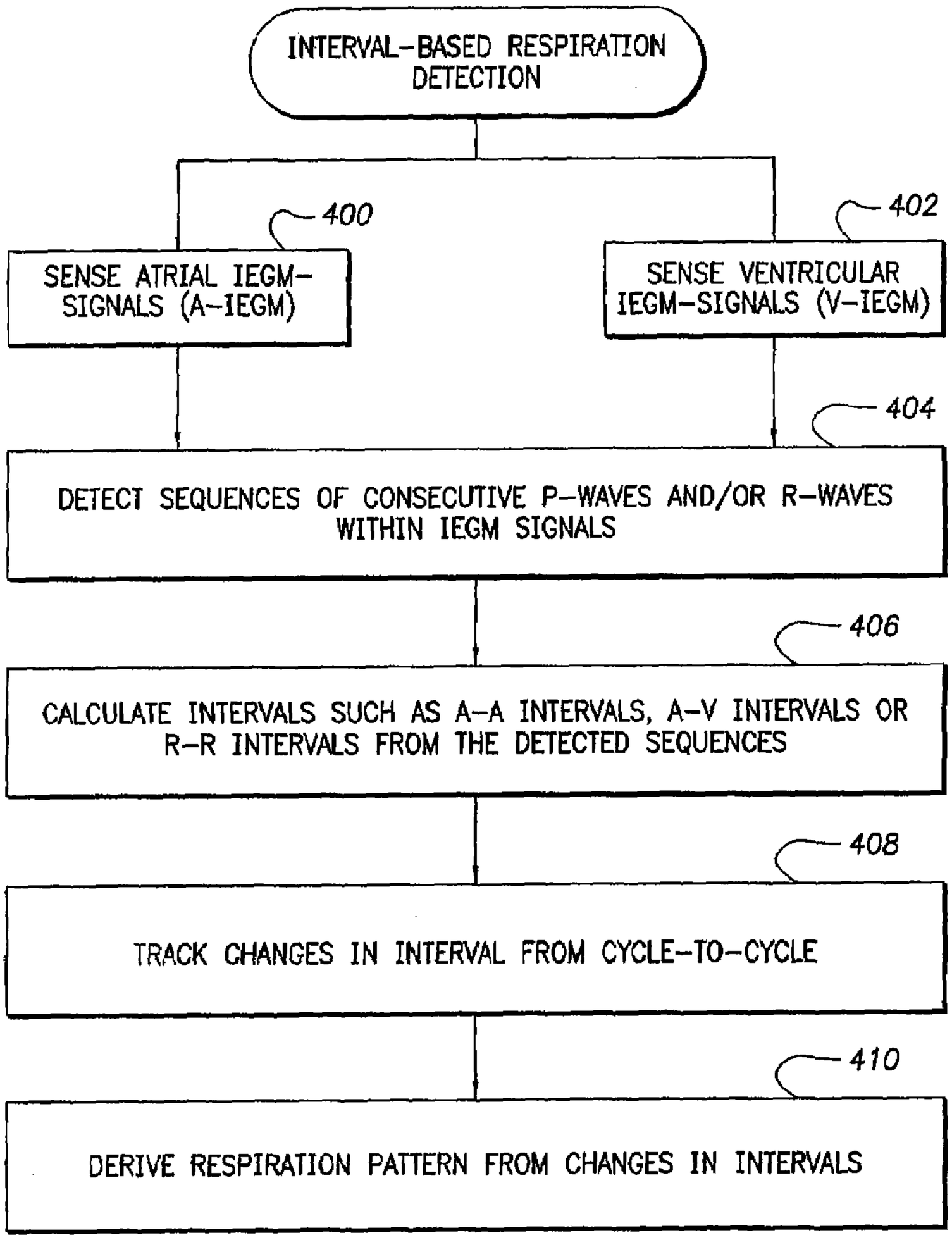

INTERVAL-BASED RESPIRATION DETECTION
400
SENSE ATRIAL IEGM-SIGNALS (A-IEGM)
402
SENSE VENTRICULAR IEGM-SIGNALS (V-IEGM)
404
DETECT SEQUENCES OF CONSECUTIVE P-WAVES AND/OR R-WAVES WITHIN IEGM SIGNALS
406
CALCULATE INTERVALS SUCH AS A-A INTERVALS, A-V INTERVALS OR R-R INTERVALS FROM THE DETECTED SEQUENCES
408
TRACK CHANGES IN INTERVAL FROM CYCLE-TO-CYCLE
410
DERIVE RESPIRATION PATTERN FROM CHANGES IN INTERVALS

FIG. 13

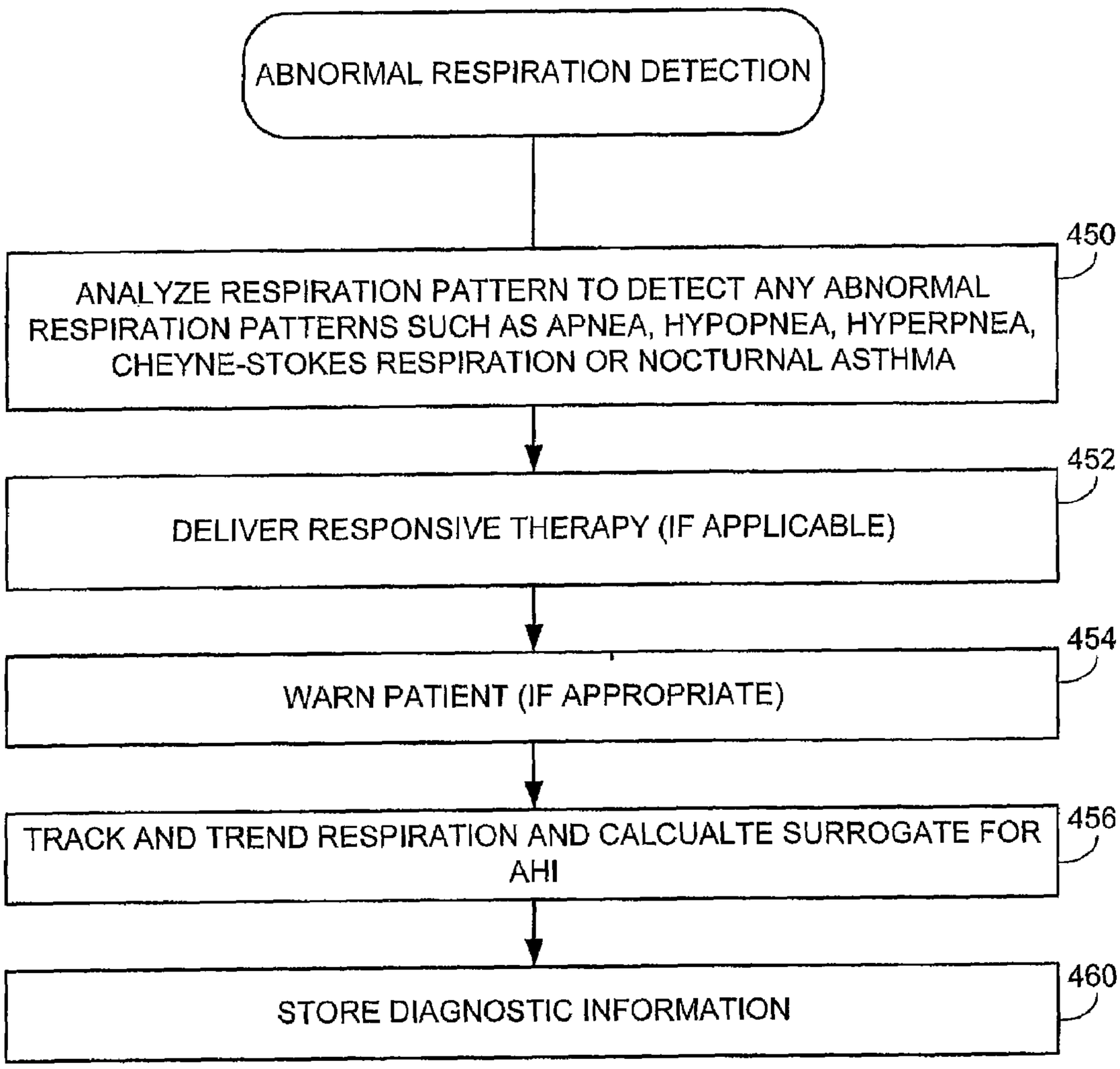

ABNORMAL RESPIRATION DETECTION
ANALYZE RESPIRATION PATTERN TO DETECT ANY ABNORMAL RESPIRATION PATTERNS SUCH AS APNEA, HYPOPNEA, HYPERPNEA, CHEYNE-STOKES RESPIRATION OR NOCTURNAL ASTHMA
450
DELIVER RESPONSIVE THERAPY (IF APPLICABLE)
452
WARN PATIENT (IF APPROPRIATE)
454
TRACK AND TREND RESPIRATION AND CALCUALTE SURROGATE FOR AHI
456
STORE DIAGNOSTIC INFORMATION
460

FIG. 14

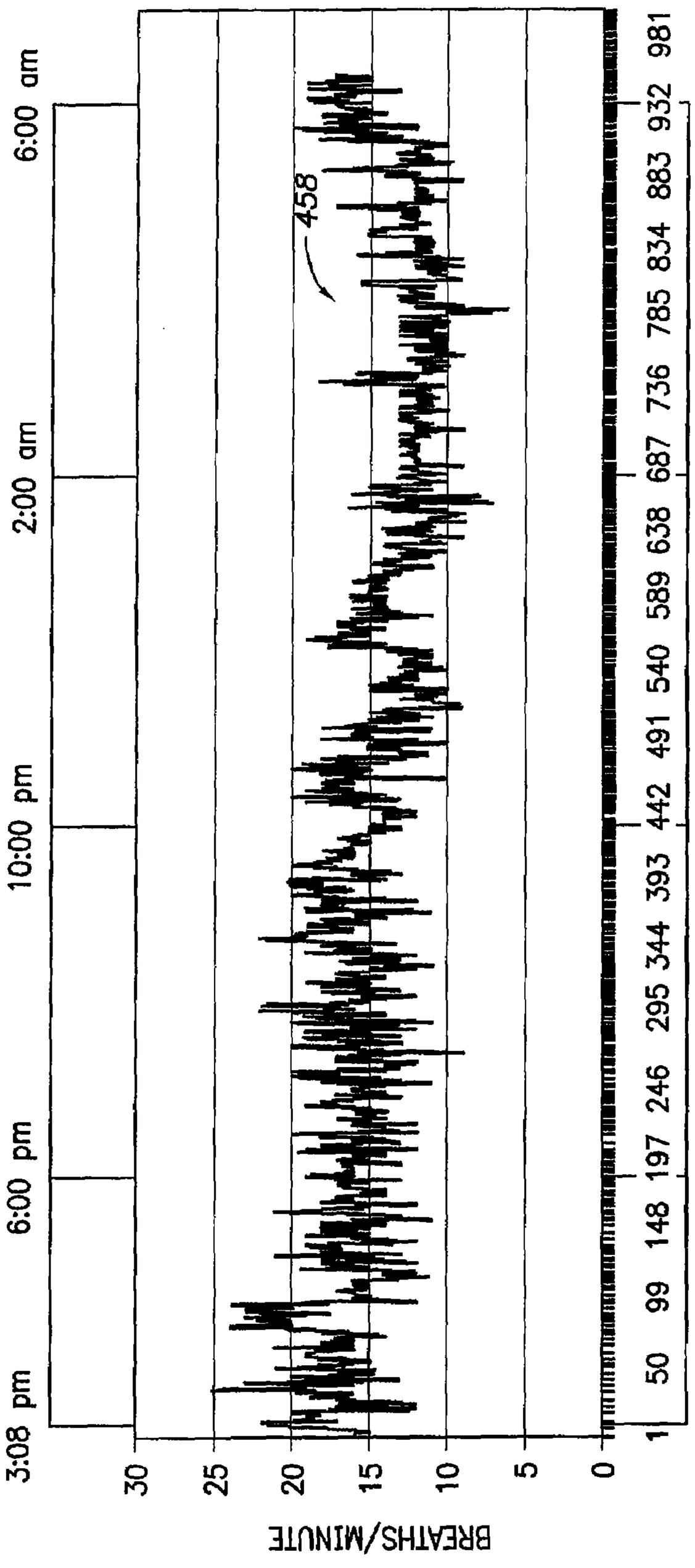

BREATHING PROFILE
6:00 am
2:00 am
10:00 pm
6:00 pm
3:08 pm
458
BREATHS/MINUTE
30
25
20
15
10
5
0
MINUTES
1
50
99
148
197
246
295
344
393
442
491
540
589
638
687
736
785
834
883
932
981

FIG. 15

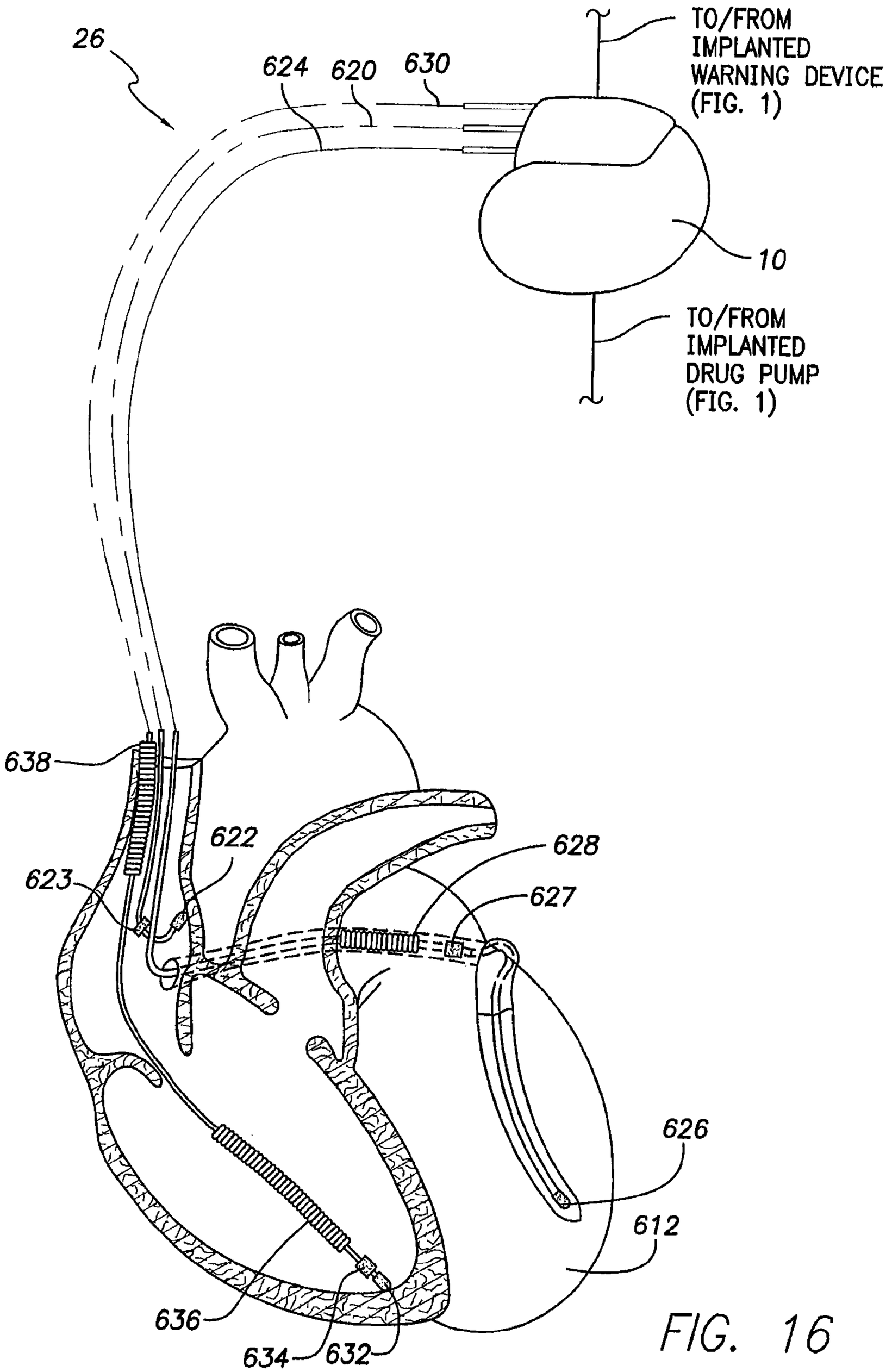

26
624
620
630
TO/FROM IMPLANTED WARNING DEVICE (FIG. 1)
10
TO/FROM IMPLANTED DRUG PUMP (FIG. 1)
638
622
623
628
627
626
612
636
634
632

FIG. 16

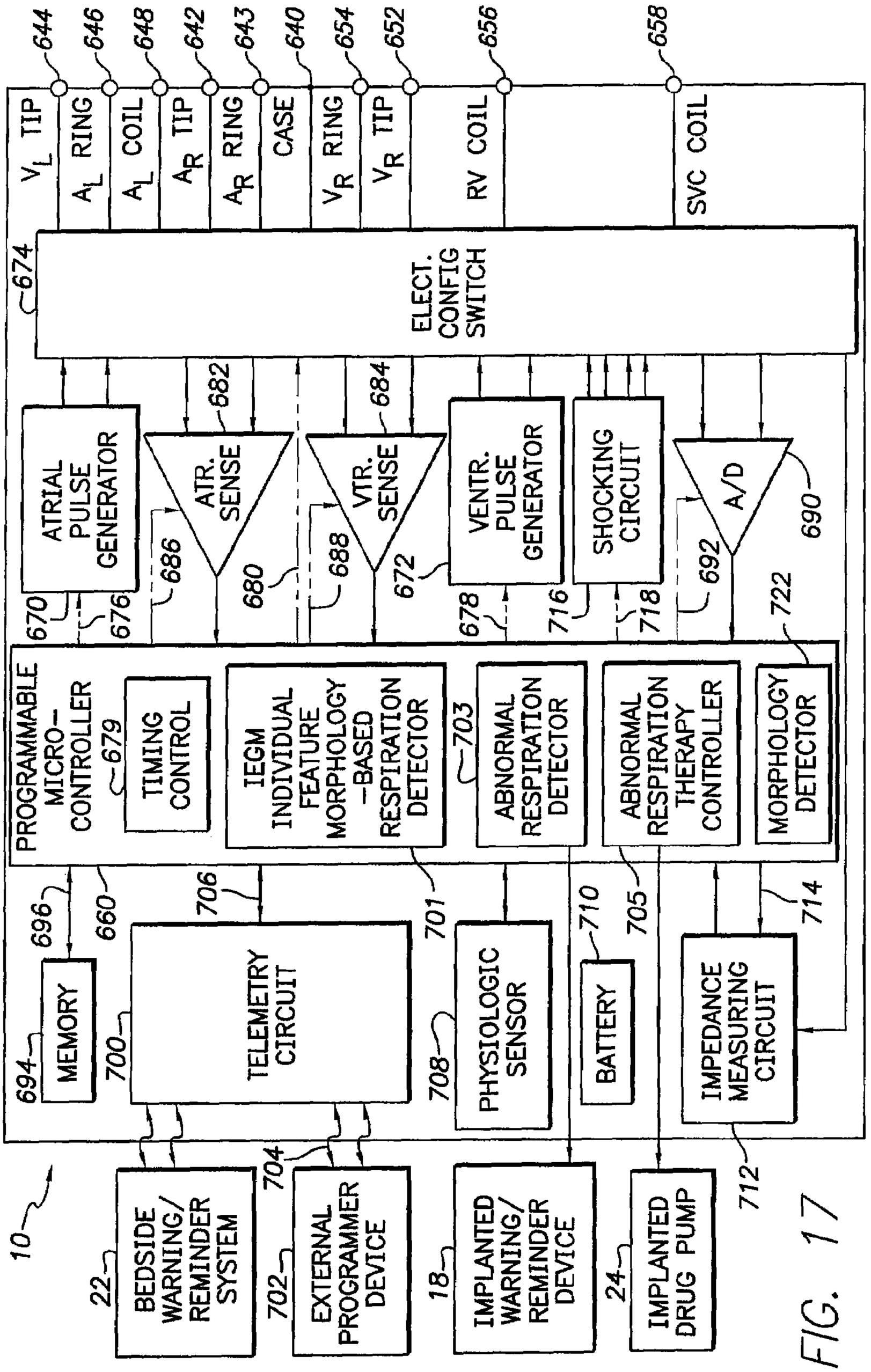

644
646
648
642
643
640
654
652
656
658
V_L TIP
A_L RING
A_L COIL
A_R TIP
A_R RING
CASE
V_R RING
V_R TIP
RV COIL
SVC COIL
674
ELECT. CONFIG SWITCH
682
684
ATRIAL PULSE GENERATOR
ATR. SENSE
VTR. SENSE
VENTR. PULSE GENERATOR
SHOCKING CIRCUIT
A/D
686
688
680
672
692
690
670
676
678
716
718
722
PROGRAMMABLE MICRO-CONTROLLER
679
TIMING CONTROL
IEGM INDIVIDUAL FEATURE MORPHOLOGY -BASED RESPIRATION DETECTOR
703
ABNORMAL RESPIRATION DETECTOR
ABNORMAL RESPIRATION THERAPY CONTROLLER
MORPHOLOGY DETECTOR
696
660
706
701
710
705
714
MEMORY
TELEMETRY CIRCUIT
PHYSIOLOGIC SENSOR
BATTERY
IMPEDANCE MEASURING CIRCUIT
694
700
708
712
10
22
704
18
24
BEDSIDE WARNING/ REMINDER SYSTEM
EXTERNAL PROGRAMMER DEVICE
IMPLANTED WARNING/ REMINDER DEVICE
IMPLANTED DRUG PUMP
702

FIG. 17

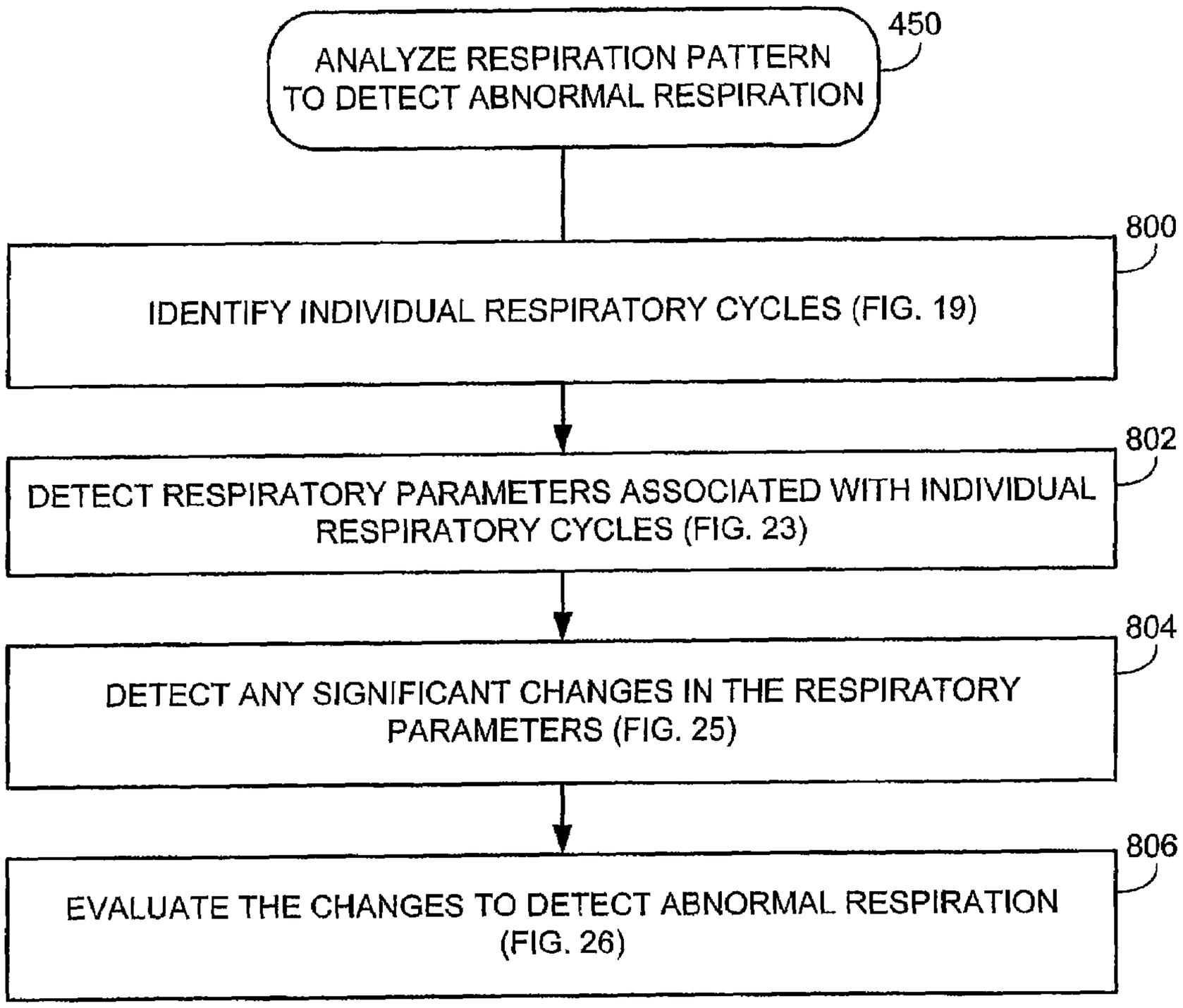

ANALYZE RESPIRATION PATTERN TO DETECT ABNORMAL RESPIRATION
450
IDENTIFY INDIVIDUAL RESPIRATORY CYCLES (FIG. 19)
800
DETECT RESPIRATORY PARAMETERS ASSOCIATED WITH INDIVIDUAL RESPIRATORY CYCLES (FIG. 23)
802
DETECT ANY SIGNIFICANT CHANGES IN THE RESPIRATORY PARAMETERS (FIG. 25)
804
EVALUATE THE CHANGES TO DETECT ABNORMAL RESPIRATION (FIG. 26)
806

FIG. 18

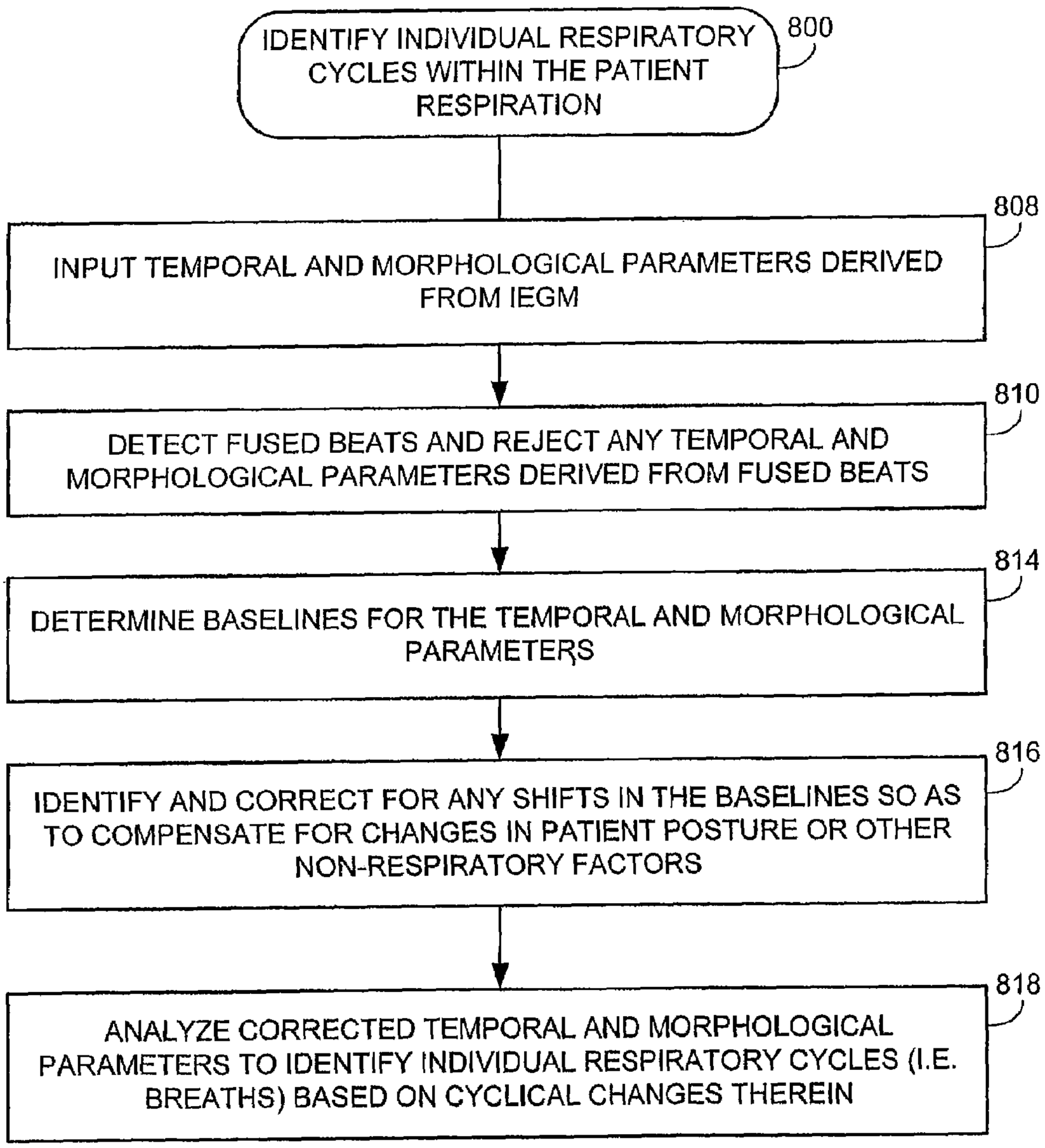

IDENTIFY INDIVIDUAL RESPIRATORY CYCLES WITHIN THE PATIENT RESPIRATION
800
INPUT TEMPORAL AND MORPHOLOGICAL PARAMETERS DERIVED FROM IEGM
808
DETECT FUSED BEATS AND REJECT ANY TEMPORAL AND MORPHOLOGICAL PARAMETERS DERIVED FROM FUSED BEATS
810
DETERMINE BASELINES FOR THE TEMPORAL AND MORPHOLOGICAL PARAMETERS
814
IDENTIFY AND CORRECT FOR ANY SHIFTS IN THE BASELINES SO AS TO COMPENSATE FOR CHANGES IN PATIENT POSTURE OR OTHER NON-RESPIRATORY FACTORS
816
ANALYZE CORRECTED TEMPORAL AND MORPHOLOGICAL PARAMETERS TO IDENTIFY INDIVIDUAL RESPIRATORY CYCLES (I.E. BREATHS) BASED ON CYCLICAL CHANGES THEREIN
818

FIG. 19

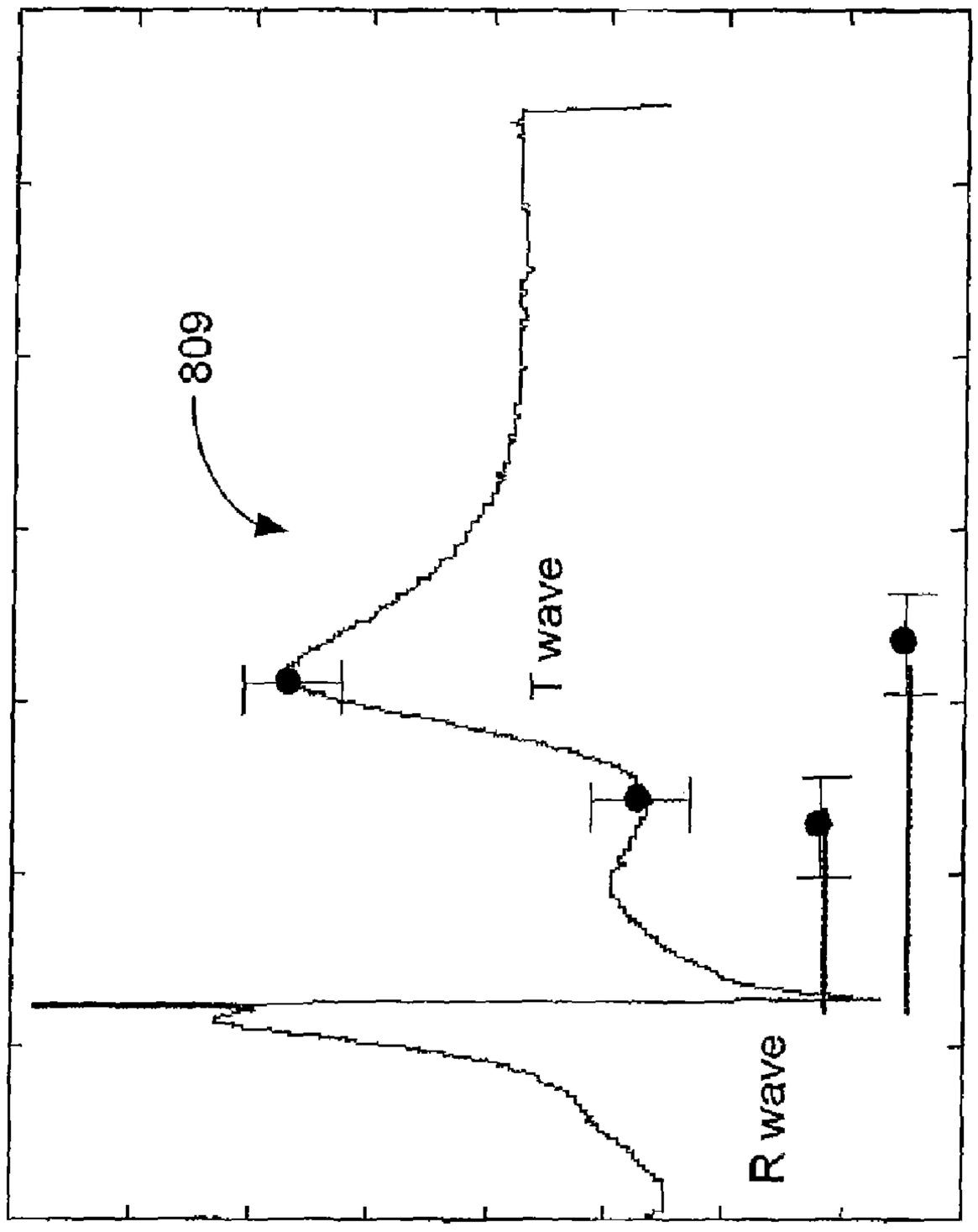


FIG. 20

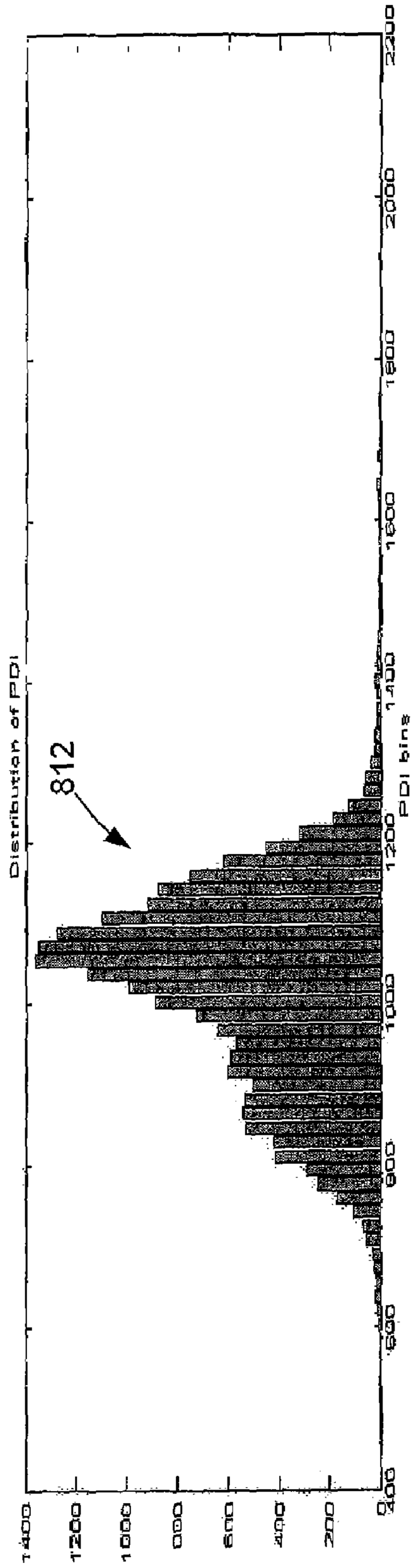

Distribution of PDI
812
PDI bins
400
600
800
1000
1200
1400
1600
1800
2000
2200
200
400
600
800
1000
1200
1400

FIG. 21

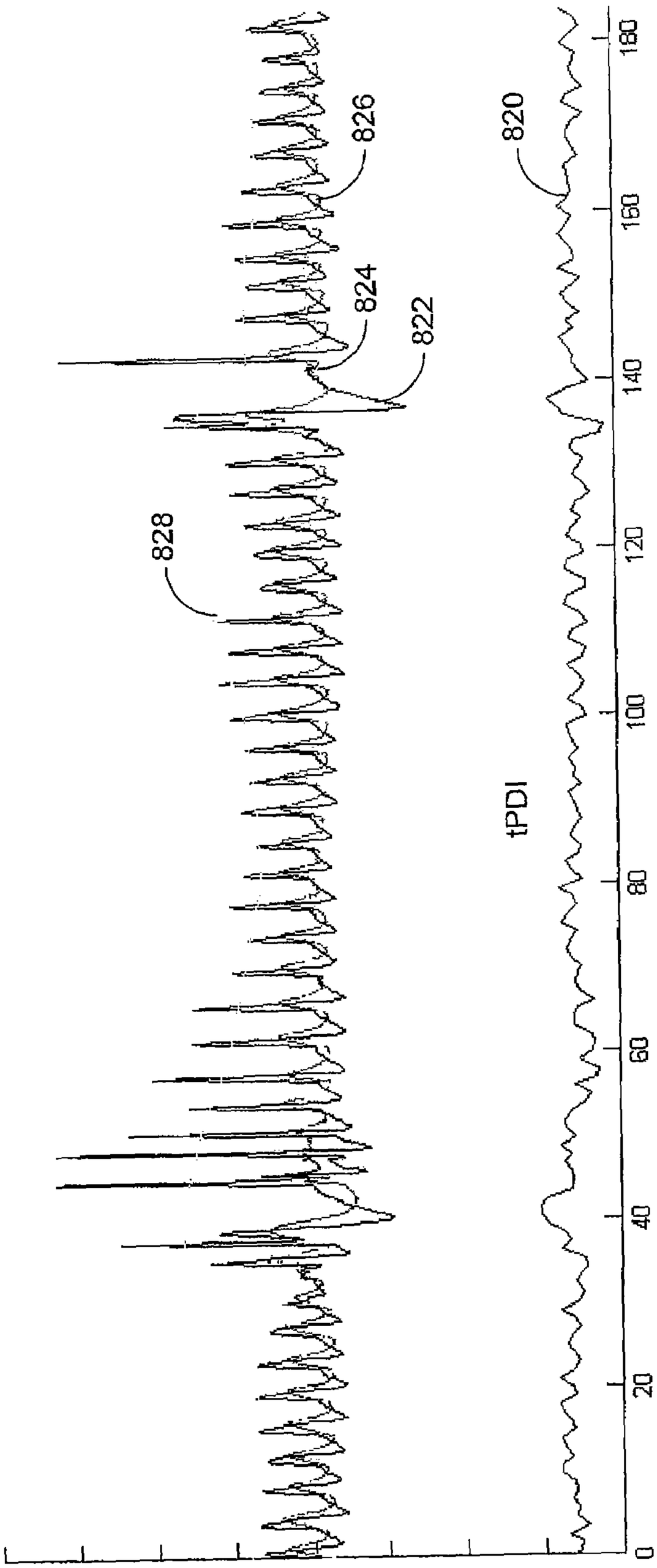

826
824
822
828
820
tPDI
seconds
180
160
140
120
100
80
60
40
20
0

FIG. 22

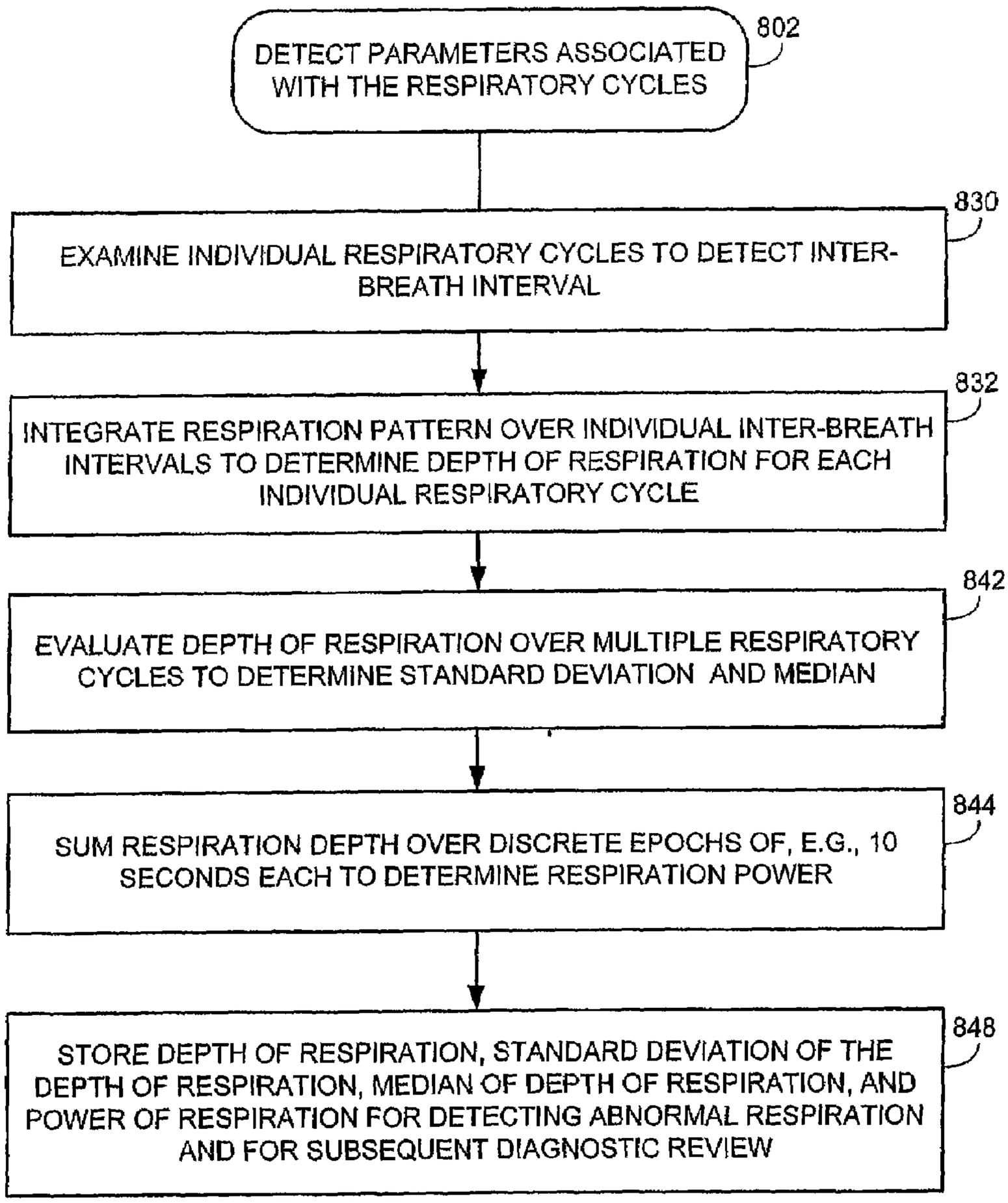

DETECT PARAMETERS ASSOCIATED WITH THE RESPIRATORY CYCLES
802
EXAMINE INDIVIDUAL RESPIRATORY CYCLES TO DETECT INTER-BREATH INTERVAL
830
INTEGRATE RESPIRATION PATTERN OVER INDIVIDUAL INTER-BREATH INTERVALS TO DETERMINE DEPTH OF RESPIRATION FOR EACH INDIVIDUAL RESPIRATORY CYCLE
832
EVALUATE DEPTH OF RESPIRATION OVER MULTIPLE RESPIRATORY CYCLES TO DETERMINE STANDARD DEVIATION AND MEDIAN
842
SUM RESPIRATION DEPTH OVER DISCRETE EPOCHS OF, E.G., 10 SECONDS EACH TO DETERMINE RESPIRATION POWER
844
STORE DEPTH OF RESPIRATION, STANDARD DEVIATION OF THE DEPTH OF RESPIRATION, MEDIAN OF DEPTH OF RESPIRATION, AND POWER OF RESPIRATION FOR DETECTING ABNORMAL RESPIRATION AND FOR SUBSEQUENT DIAGNOSTIC REVIEW
848

FIG. 23

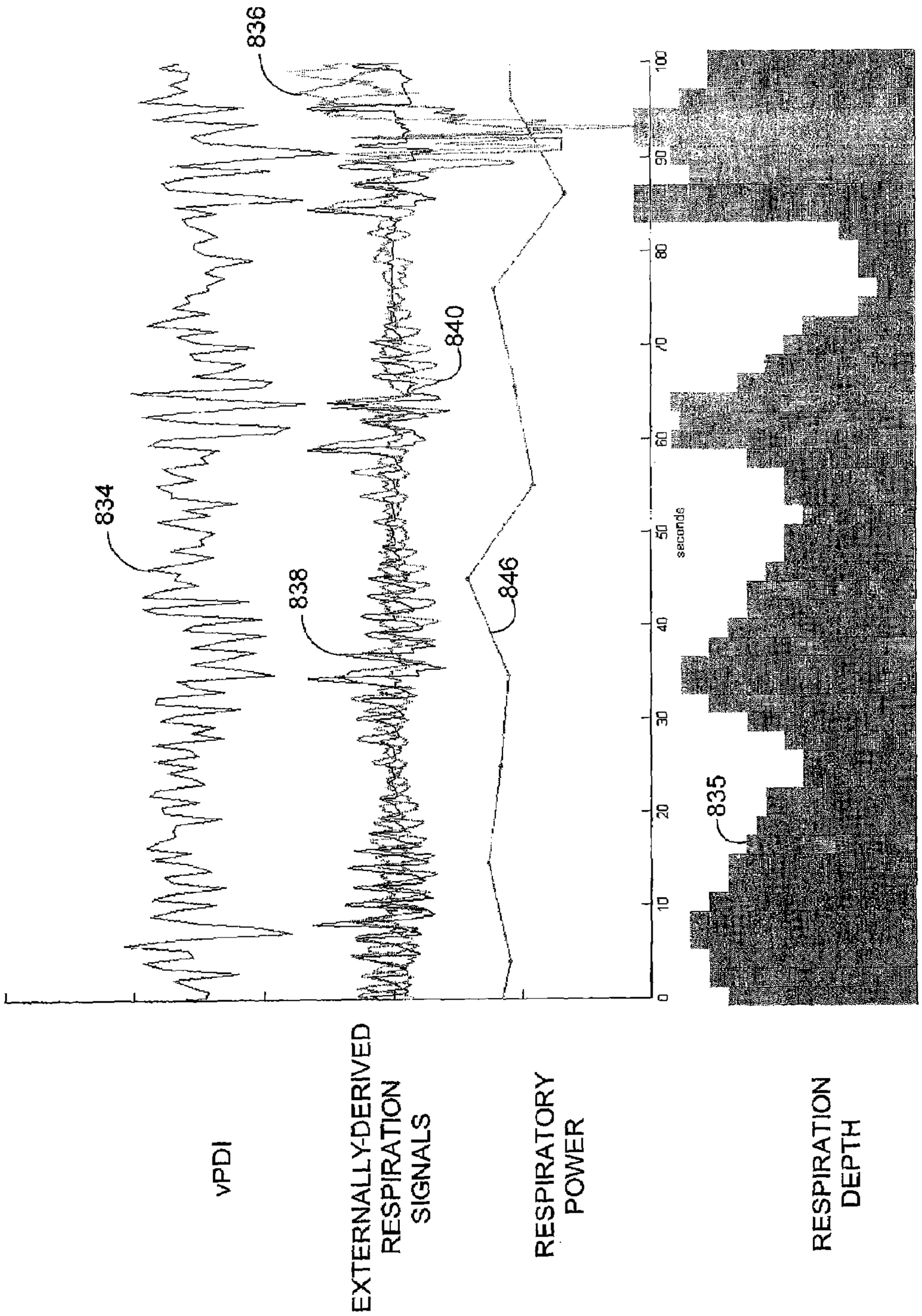

836
834
838
840
846
vPDI
EXTERNALLY-DERIVED RESPIRATION SIGNALS
RESPIRATORY POWER
RESPIRATION DEPTH
835
seconds
0
10
20
30
40
50
60
70
80
90
100

FIG. 24

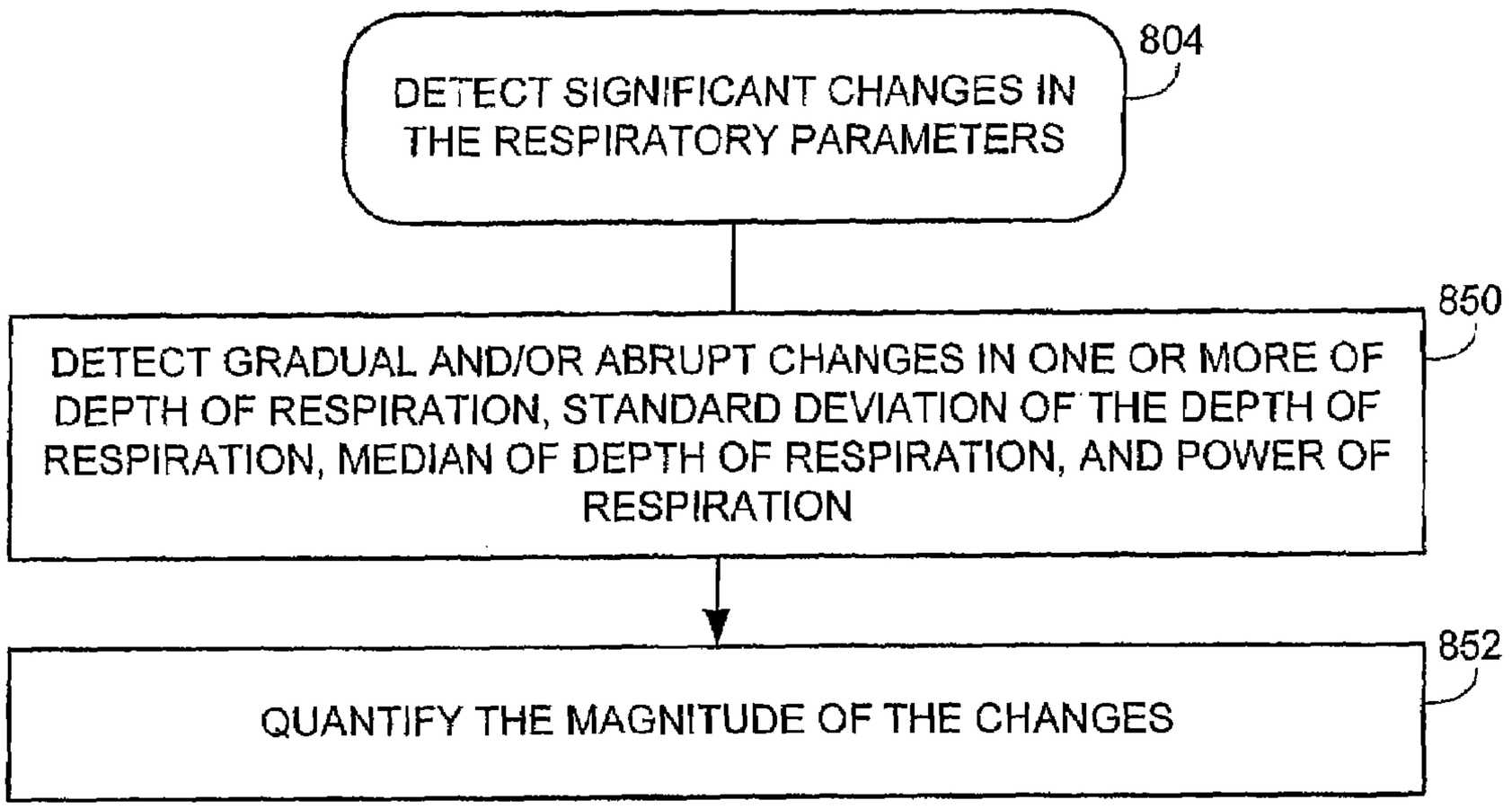

DETECT SIGNIFICANT CHANGES IN THE RESPIRATORY PARAMETERS
804
DETECT GRADUAL AND/OR ABRUPT CHANGES IN ONE OR MORE OF DEPTH OF RESPIRATION, STANDARD DEVIATION OF THE DEPTH OF RESPIRATION, MEDIAN OF DEPTH OF RESPIRATION, AND POWER OF RESPIRATION
850
QUANTIFY THE MAGNITUDE OF THE CHANGES
852

FIG. 25

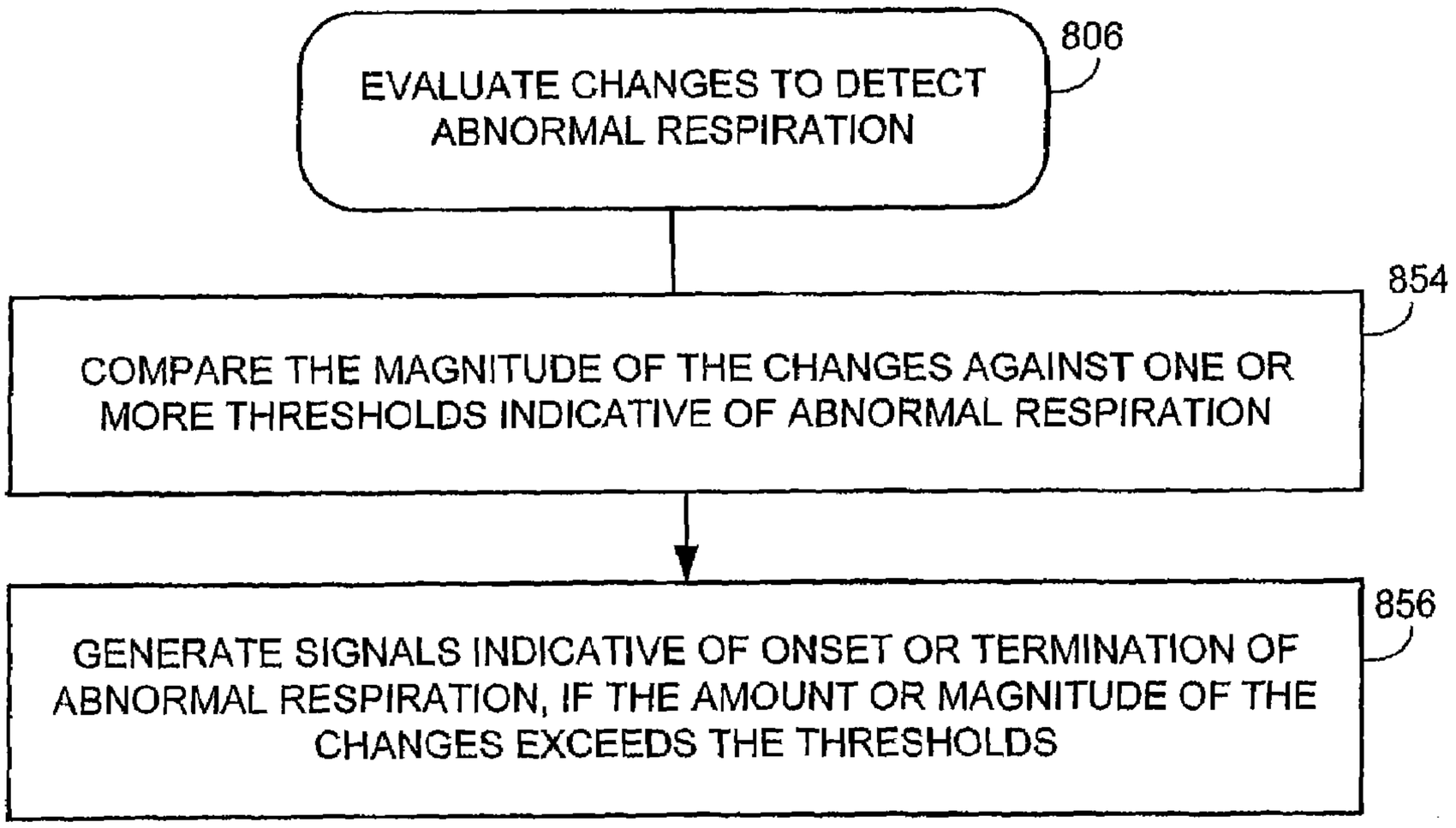

EVALUATE CHANGES TO DETECT ABNORMAL RESPIRATION
806
COMPARE THE MAGNITUDE OF THE CHANGES AGAINST ONE OR MORE THRESHOLDS INDICATIVE OF ABNORMAL RESPIRATION
854
GENERATE SIGNALS INDICATIVE OF ONSET OR TERMINATION OF ABNORMAL RESPIRATION, IF THE AMOUNT OR MAGNITUDE OF THE CHANGES EXCEEDS THE THRESHOLDS
856

FIG. 26

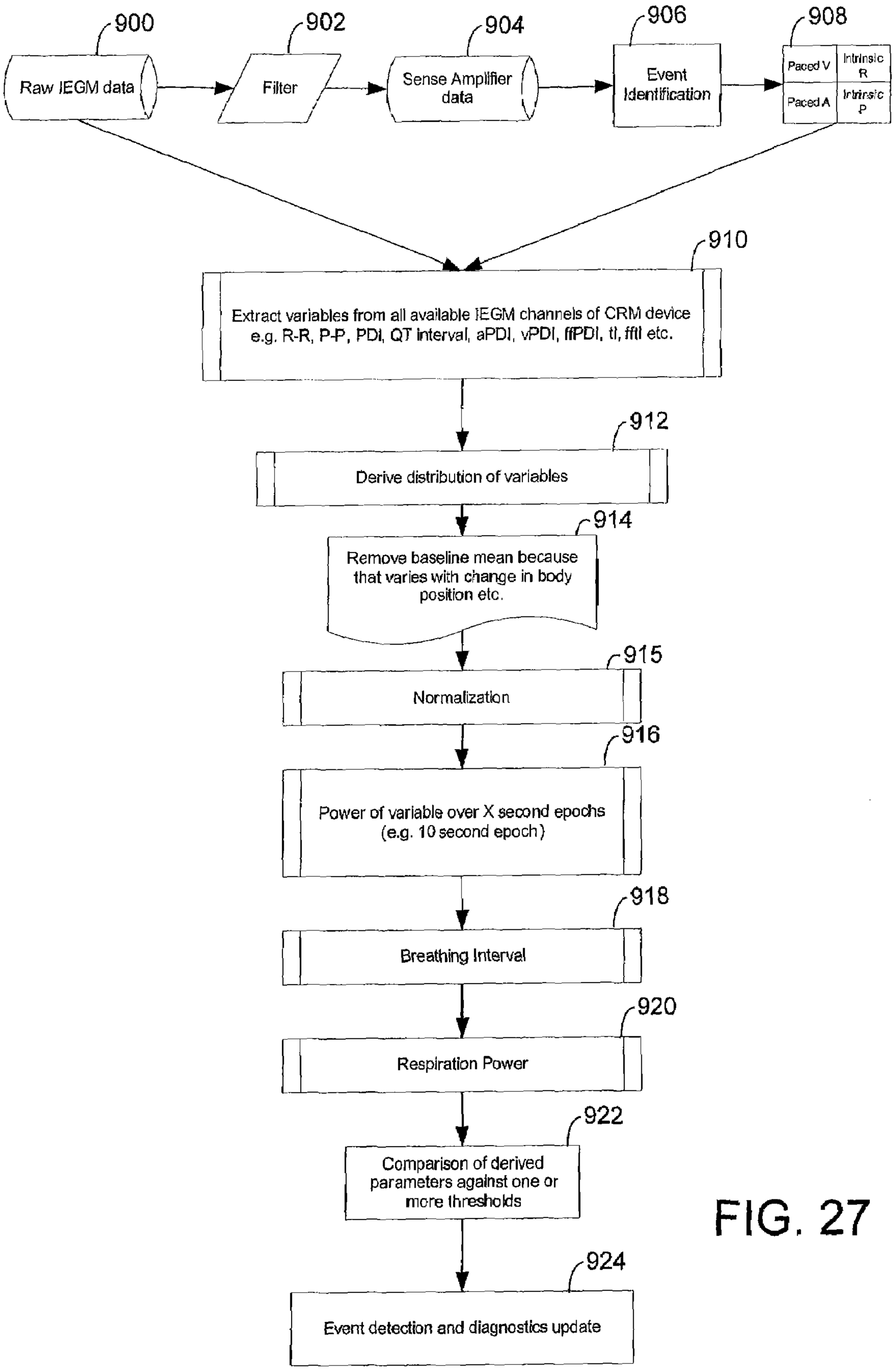

900
Raw IEGM data
902
Filter
904
Sense Amplifier data
906
Event Identification
908
Paced V
Intrinsic R
Paced A
Intrinsic P
910
Extract variables from all available IEGM channels of CRM device e.g. R-R, P-P, PDI, QT interval, aPDI, vPDI, ffPDI, tI, ffII etc.
912
Derive distribution of variables
914
Remove baseline mean because that varies with change in body position etc.
915
Normalization
916
Power of variable over X second epochs (e.g. 10 second epoch)
918
Breathing Interval
920
Respiration Power
922
Comparison of derived parameters against one or more thresholds
924
Event detection and diagnostics update

FIG. 27

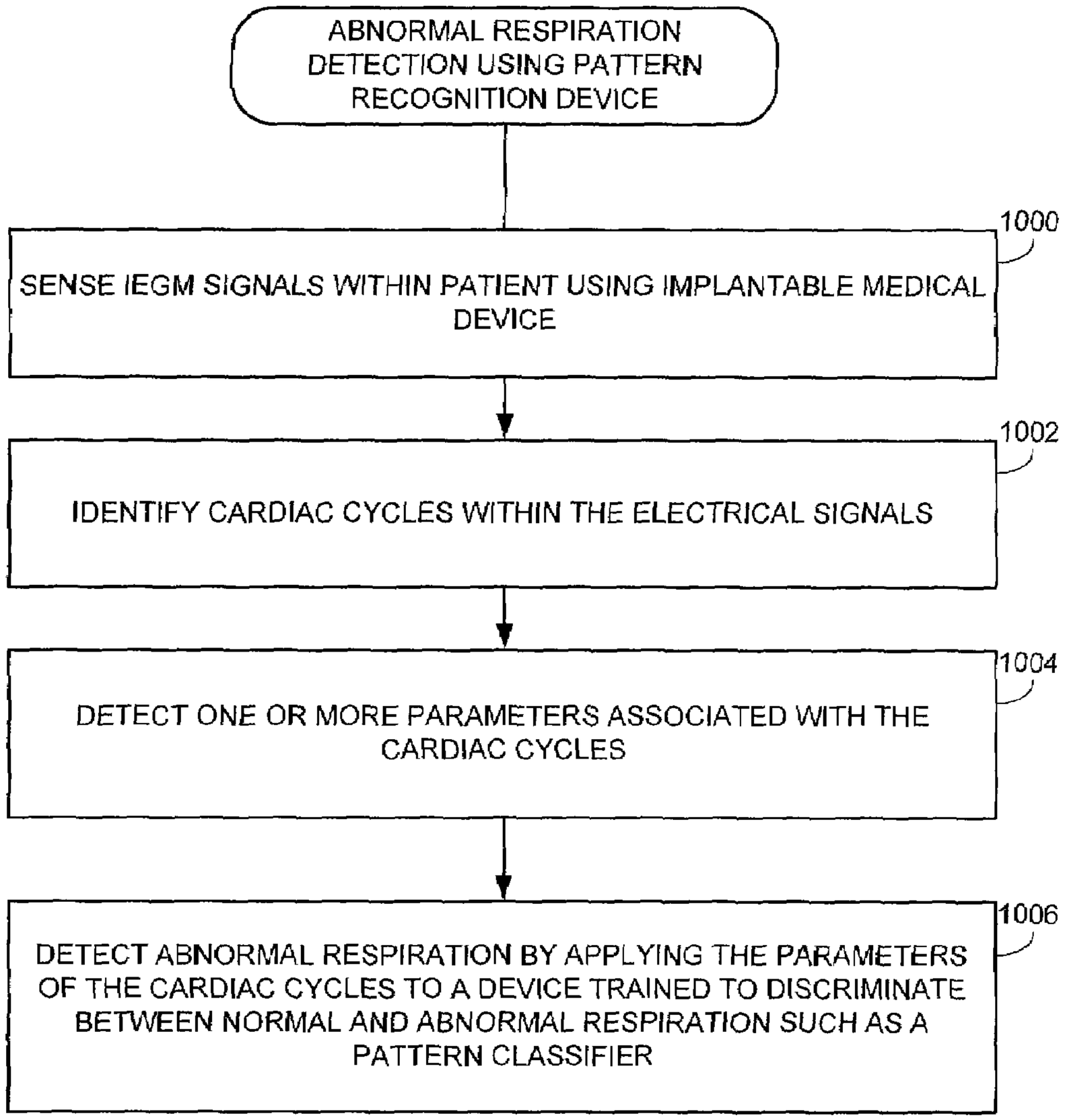

ABNORMAL RESPIRATION DETECTION USING PATTERN RECOGNITION DEVICE
1000
SENSE IEGM SIGNALS WITHIN PATIENT USING IMPLANTABLE MEDICAL DEVICE
1002
IDENTIFY CARDIAC CYCLES WITHIN THE ELECTRICAL SIGNALS
1004
DETECT ONE OR MORE PARAMETERS ASSOCIATED WITH THE CARDIAC CYCLES
1006
DETECT ABNORMAL RESPIRATION BY APPLYING THE PARAMETERS OF THE CARDIAC CYCLES TO A DEVICE TRAINED TO DISCRIMINATE BETWEEN NORMAL AND ABNORMAL RESPIRATION SUCH AS A PATTERN CLASSIFIER

FIG. 28

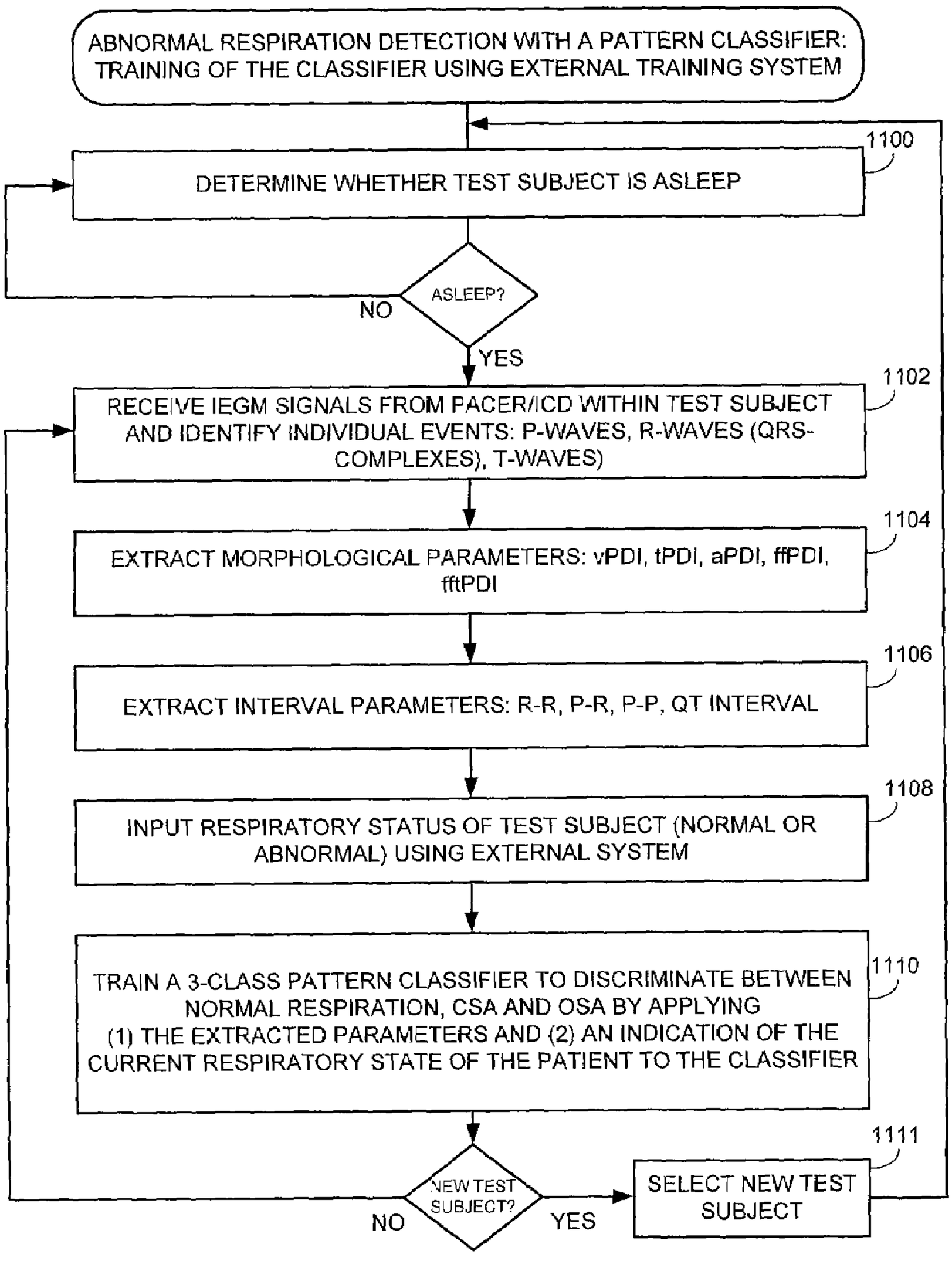

ABNORMAL RESPIRATION DETECTION WITH A PATTERN CLASSIFIER: TRAINING OF THE CLASSIFIER USING EXTERNAL TRAINING SYSTEM
1100
DETERMINE WHETHER TEST SUBJECT IS ASLEEP
ASLEEP?
NO
YES
1102
RECEIVE IEGM SIGNALS FROM PACER/ICD WITHIN TEST SUBJECT AND IDENTIFY INDIVIDUAL EVENTS: P-WAVES, R-WAVES (QRS-COMPLEXES), T-WAVES)
1104
EXTRACT MORPHOLOGICAL PARAMETERS: vPDI, tPDI, aPDI, ffPDI, fftPDI
1106
EXTRACT INTERVAL PARAMETERS: R-R, P-R, P-P, QT INTERVAL
1108
INPUT RESPIRATORY STATUS OF TEST SUBJECT (NORMAL OR ABNORMAL) USING EXTERNAL SYSTEM
1110
TRAIN A 3-CLASS PATTERN CLASSIFIER TO DISCRIMINATE BETWEEN NORMAL RESPIRATION, CSA AND OSA BY APPLYING (1) THE EXTRACTED PARAMETERS AND (2) AN INDICATION OF THE CURRENT RESPIRATORY STATE OF THE PATIENT TO THE CLASSIFIER
NEW TEST SUBJECT?
NO
YES
1111
SELECT NEW TEST SUBJECT

FIG. 29

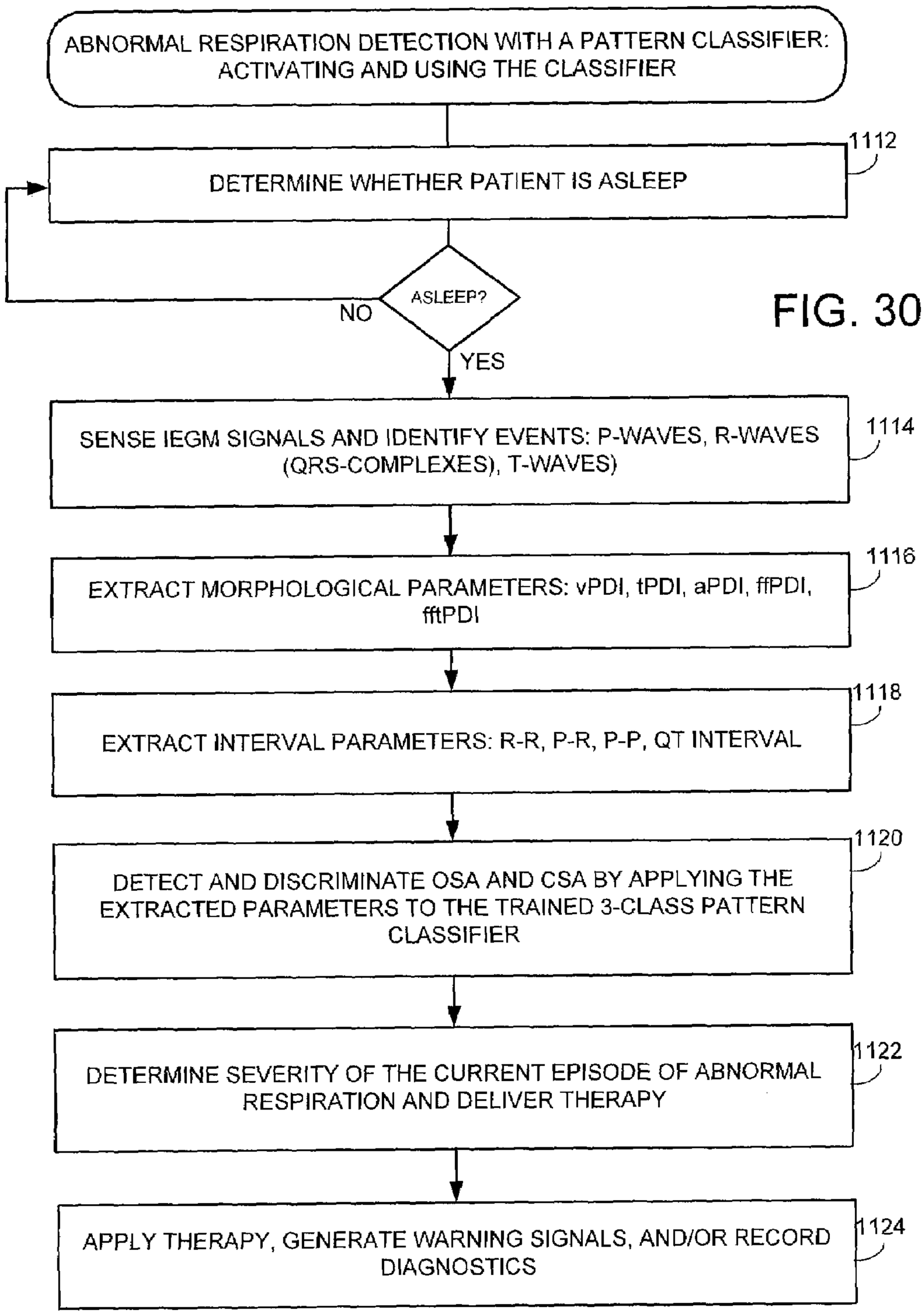

ABNORMAL RESPIRATION DETECTION WITH A PATTERN CLASSIFIER: ACTIVATING AND USING THE CLASSIFIER
DETERMINE WHETHER PATIENT IS ASLEEP
1112
ASLEEP?
NO
YES
SENSE IEGM SIGNALS AND IDENTIFY EVENTS: P-WAVES, R-WAVES (QRS-COMPLEXES), T-WAVES)
1114
EXTRACT MORPHOLOGICAL PARAMETERS: vPDI, tPDI, aPDI, ffPDI, fftPDI
1116
EXTRACT INTERVAL PARAMETERS: R-R, P-R, P-P, QT INTERVAL
1118
DETECT AND DISCRIMINATE OSA AND CSA BY APPLYING THE EXTRACTED PARAMETERS TO THE TRAINED 3-CLASS PATTERN CLASSIFIER
1120
DETERMINE SEVERITY OF THE CURRENT EPISODE OF ABNORMAL RESPIRATION AND DELIVER THERAPY
1122
APPLY THERAPY, GENERATE WARNING SIGNALS, AND/OR RECORD DIAGNOSTICS
1124

FIG. 30

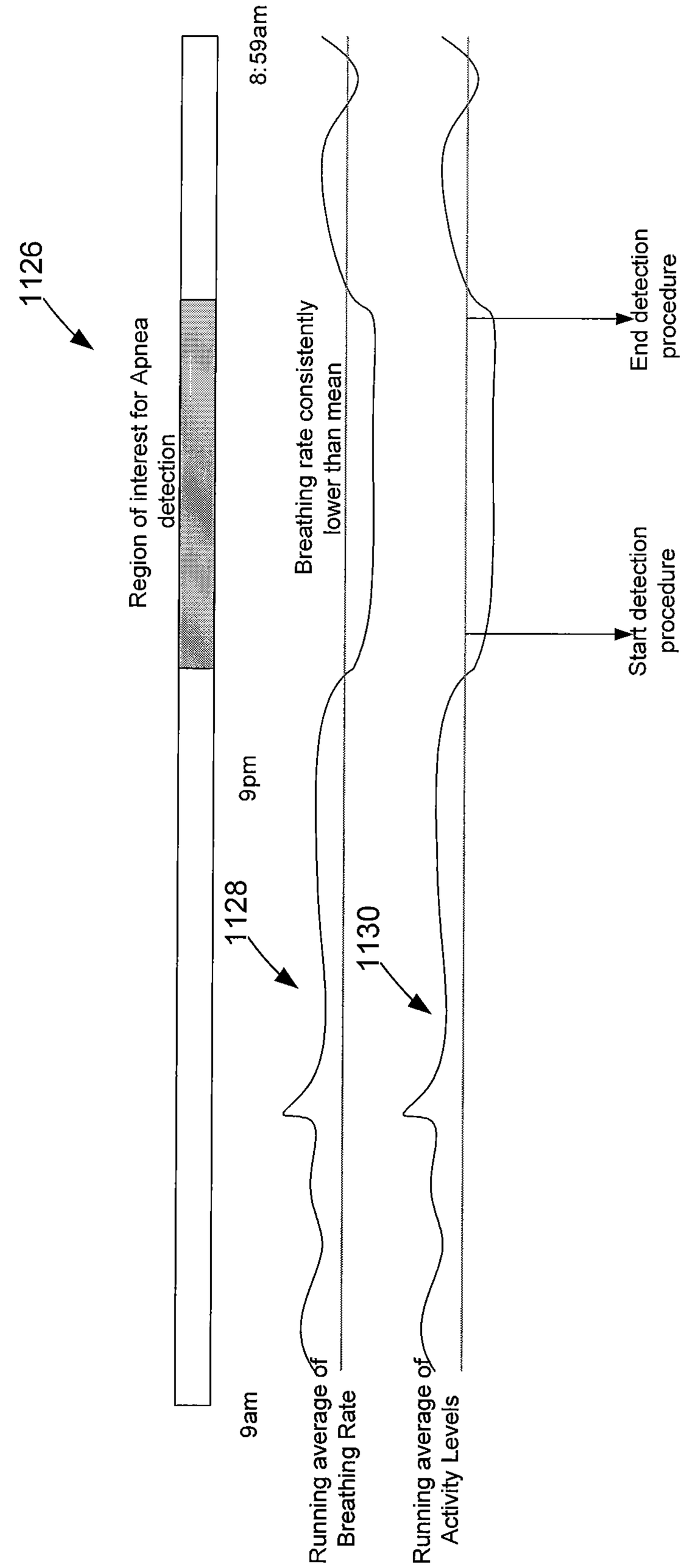

1126
Region of interest for Apnea detection
8:59am
Breathing rate consistently lower than mean
End detection procedure
9pm
1128
1130
Start detection procedure
9am
Running average of Breathing Rate
Running average of Activity Levels

FIG. 31

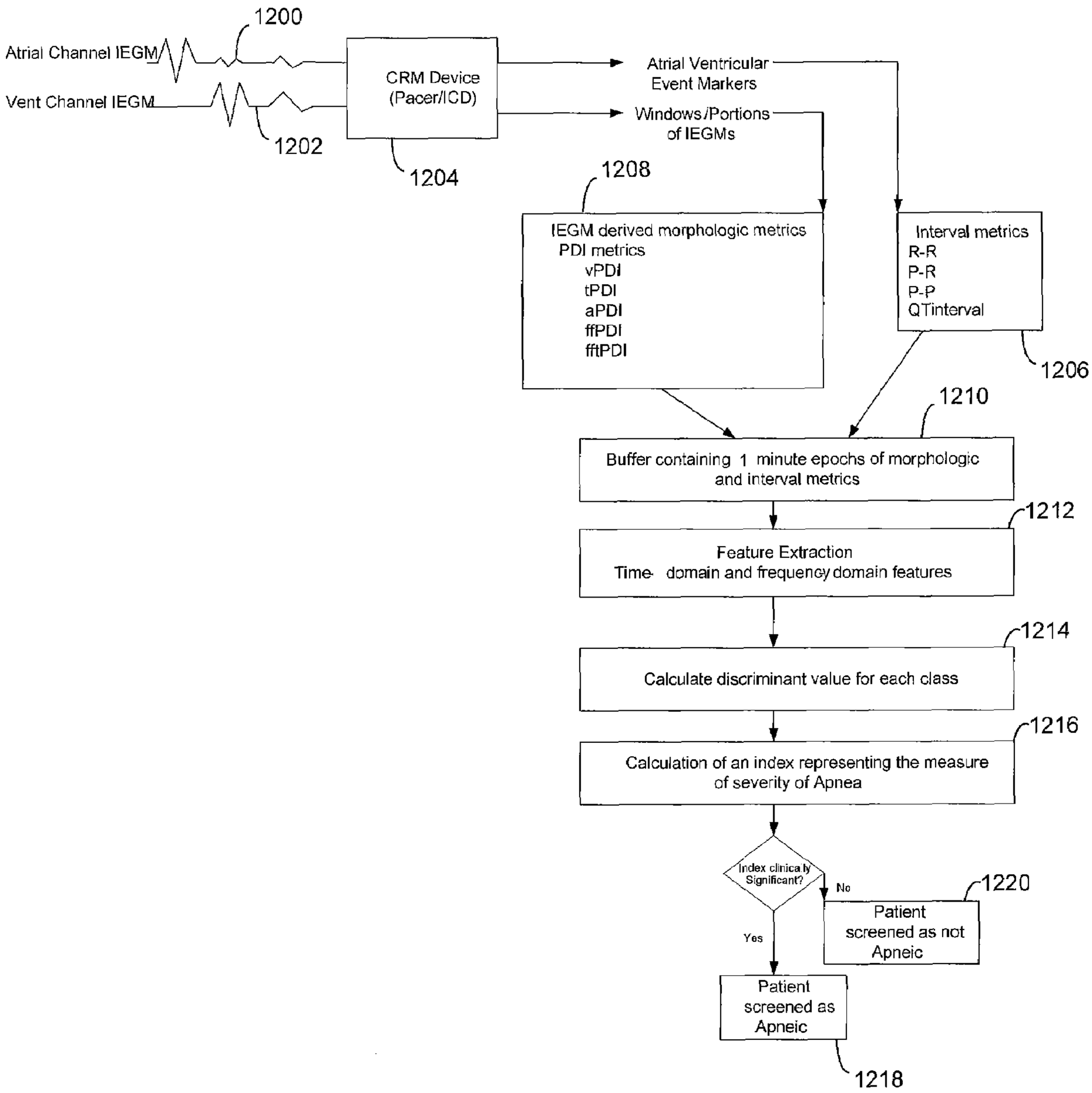

1200
Atrial Channel IEGM
Vent Channel IEGM
1202
CRM Device
(Pacer/ICD)
1204
Atrial Ventricular
Event Markers
Windows/Portions
of IEGMs
1208
IEGM derived morphologic metrics
PDI metrics
vPDI
tPDI
aPDI
ffPDI
fftPDI
Interval metrics
R-R
P-R
P-P
QTinterval
1206
1210
Buffer containing 1 minute epochs of morphologic
and interval metrics
1212
Feature Extraction
Time- domain and frequency domain features
1214
Calculate discriminant value for each class
1216
Calculation of an index representing the measure
of severity of Apnea
Index clinically
Significant?
No
1220
Patient
screened as not
Apneic
Yes
Patient
screened as
Apneic
1218

FIG. 32

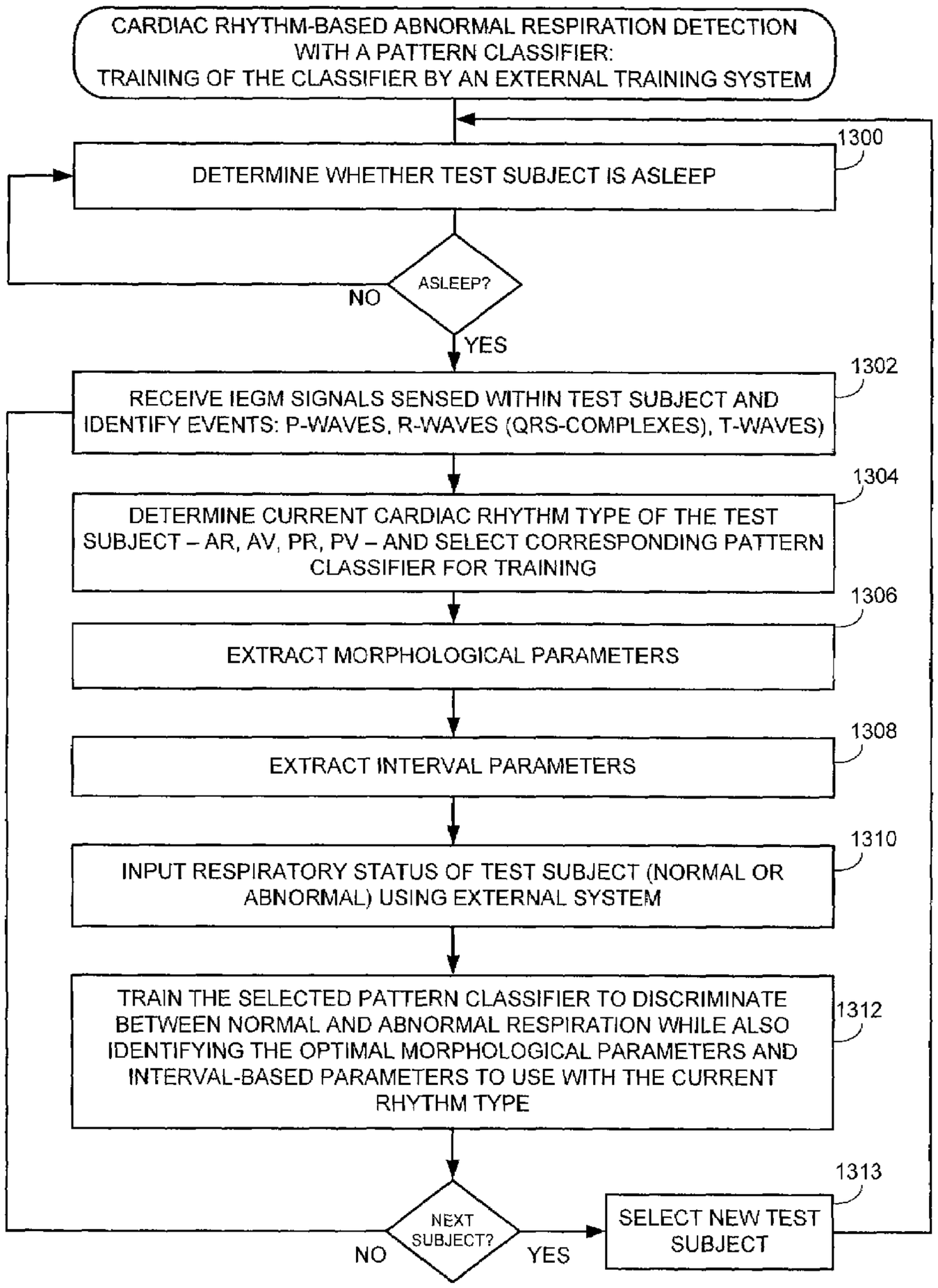

CARDIAC RHYTHM-BASED ABNORMAL RESPIRATION DETECTION WITH A PATTERN CLASSIFIER: TRAINING OF THE CLASSIFIER BY AN EXTERNAL TRAINING SYSTEM
1300
DETERMINE WHETHER TEST SUBJECT IS ASLEEP
ASLEEP?
NO
YES
1302
RECEIVE IEGM SIGNALS SENSED WITHIN TEST SUBJECT AND IDENTIFY EVENTS: P-WAVES, R-WAVES (QRS-COMPLEXES), T-WAVES)
1304
DETERMINE CURRENT CARDIAC RHYTHM TYPE OF THE TEST SUBJECT – AR, AV, PR, PV – AND SELECT CORRESPONDING PATTERN CLASSIFIER FOR TRAINING
1306
EXTRACT MORPHOLOGICAL PARAMETERS
1308
EXTRACT INTERVAL PARAMETERS
1310
INPUT RESPIRATORY STATUS OF TEST SUBJECT (NORMAL OR ABNORMAL) USING EXTERNAL SYSTEM
1312
TRAIN THE SELECTED PATTERN CLASSIFIER TO DISCRIMINATE BETWEEN NORMAL AND ABNORMAL RESPIRATION WHILE ALSO IDENTIFYING THE OPTIMAL MORPHOLOGICAL PARAMETERS AND INTERVAL-BASED PARAMETERS TO USE WITH THE CURRENT RHYTHM TYPE
1313
NEXT SUBJECT?
NO
YES
SELECT NEW TEST SUBJECT

FIG. 33

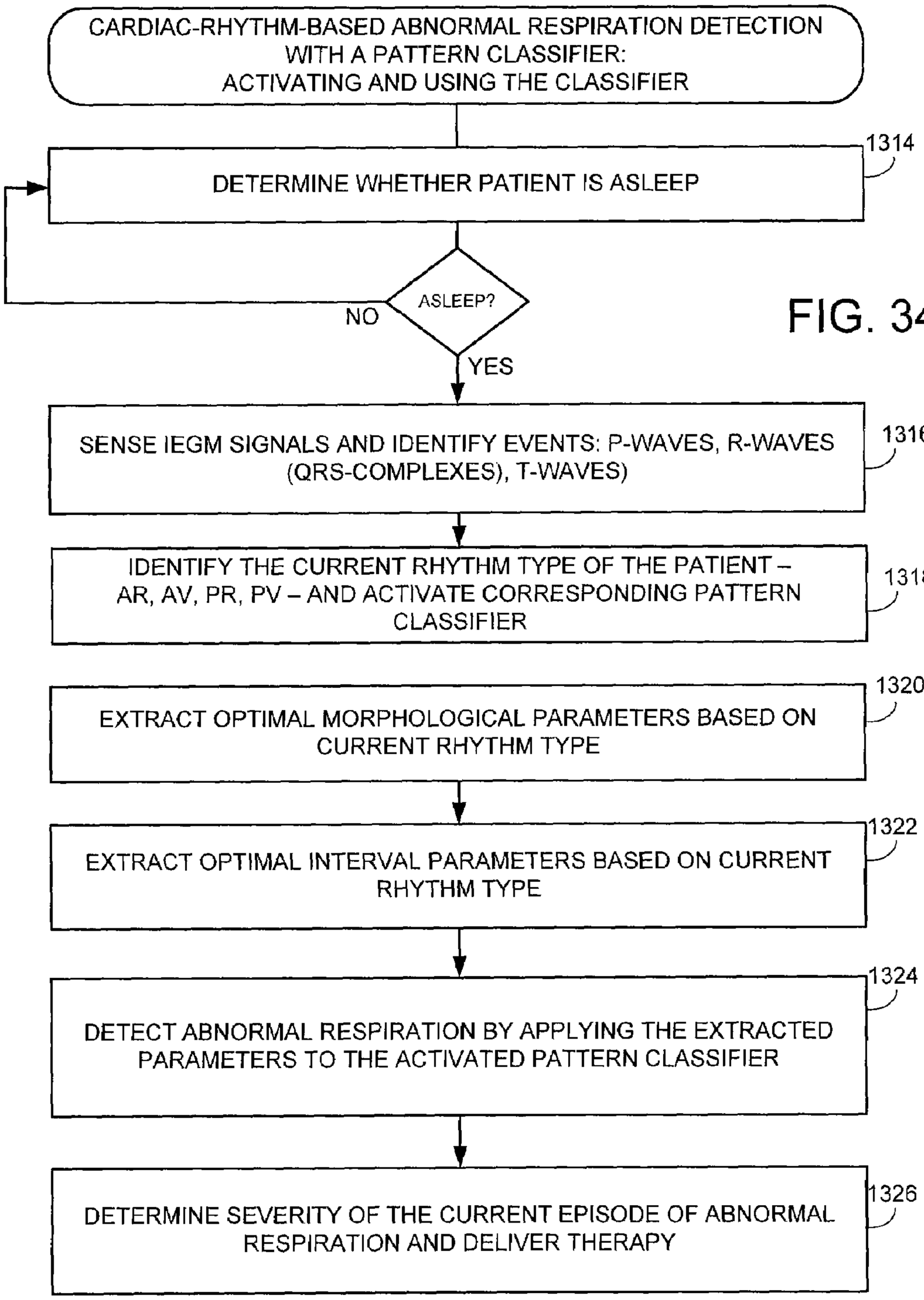

CARDIAC-RHYTHM-BASED ABNORMAL RESPIRATION DETECTION WITH A PATTERN CLASSIFIER: ACTIVATING AND USING THE CLASSIFIER
DETERMINE WHETHER PATIENT IS ASLEEP
1314
ASLEEP?
NO
YES
SENSE IEGM SIGNALS AND IDENTIFY EVENTS: P-WAVES, R-WAVES (QRS-COMPLEXES), T-WAVES)
1316
IDENTIFY THE CURRENT RHYTHM TYPE OF THE PATIENT – AR, AV, PR, PV – AND ACTIVATE CORRESPONDING PATTERN CLASSIFIER
1318
EXTRACT OPTIMAL MORPHOLOGICAL PARAMETERS BASED ON CURRENT RHYTHM TYPE
1320
EXTRACT OPTIMAL INTERVAL PARAMETERS BASED ON CURRENT RHYTHM TYPE
1322
DETECT ABNORMAL RESPIRATION BY APPLYING THE EXTRACTED PARAMETERS TO THE ACTIVATED PATTERN CLASSIFIER
1324
DETERMINE SEVERITY OF THE CURRENT EPISODE OF ABNORMAL RESPIRATION AND DELIVER THERAPY
1326

FIG. 34

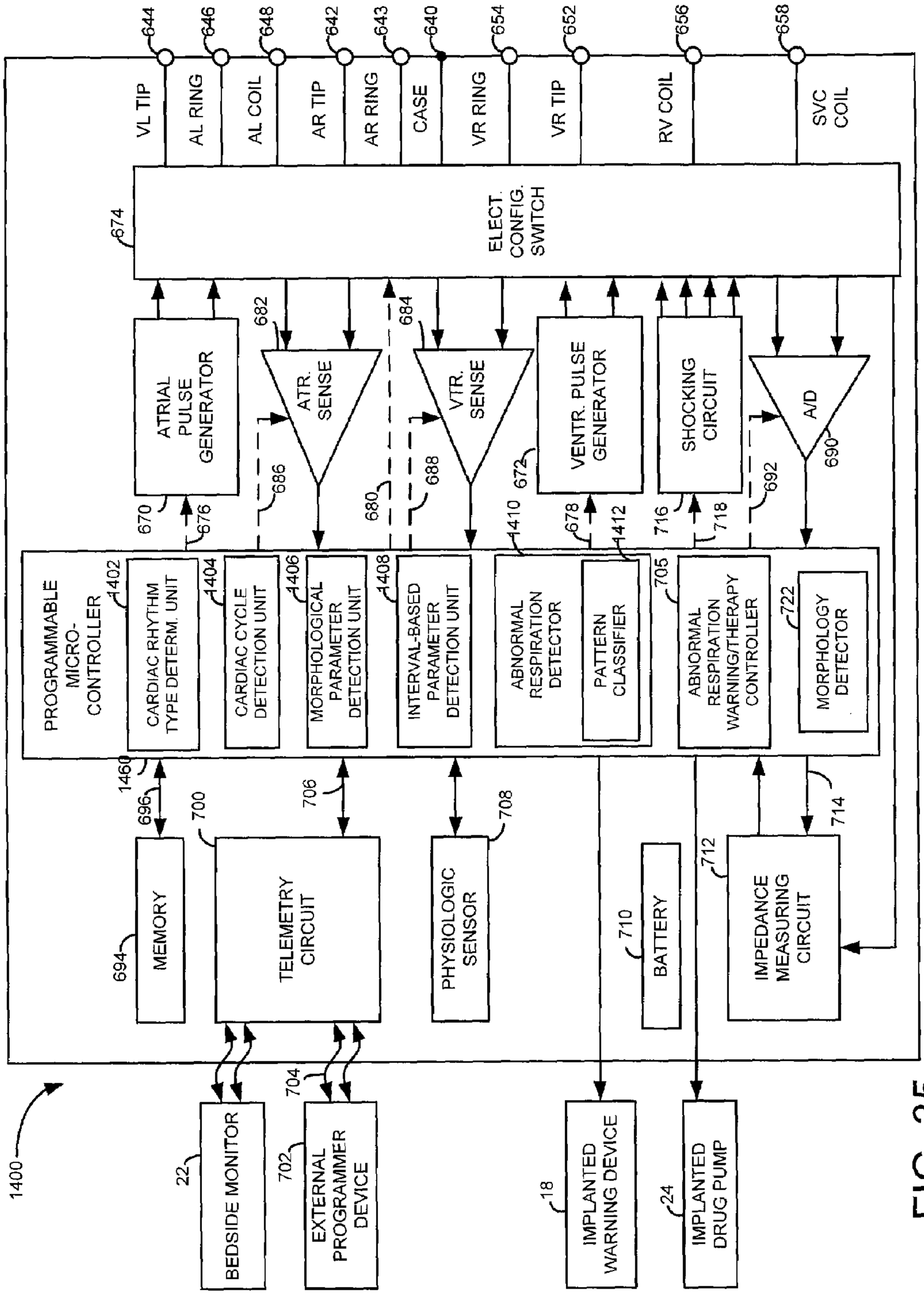

644
646
648
642
643
640
654
652
656
658
VL TIP
AL RING
AL COIL
AR TIP
AR RING
CASE
VR RING
VR TIP
RV COIL
SVC COIL
674
ELECT. CONFIG. SWITCH
682
684
ATRIAL PULSE GENERATOR
ATR. SENSE
VTR. SENSE
VENTR. PULSE GENERATOR
SHOCKING CIRCUIT
A/D
670
676
686
680
688
672
678
1410
1412
716
718
692
690
PROGRAMMABLE MICRO-CONTROLLER
1402
CARDIAC RHYTHM TYPE DETERM. UNIT
1404
CARDIAC CYCLE DETECTION UNIT
1406
MORPHOLOGICAL PARAMETER DETECTION UNIT
1408
INTERVAL-BASED PARAMETER DETECTION UNIT
ABNORMAL RESPIRATION DETECTOR
PATTERN CLASSIFIER
705
ABNORMAL RESPIRATION WARNING/THERAPY CONTROLLER
722
MORPHOLOGY DETECTOR
1460
696
700
706
708
714
712
MEMORY
TELEMETRY CIRCUIT
PHYSIOLOGIC SENSOR
BATTERY
IMPEDANCE MEASURING CIRCUIT
694
710
704
1400
22
BEDSIDE MONITOR
702
EXTERNAL PROGRAMMER DEVICE
18
IMPLANTED WARNING DEVICE
24
IMPLANTED DRUG PUMP

FIG. 35

SYSTEM AND METHOD FOR DETECTING ABNORMAL RESPIRATION BASED ON INTRACARDIAC ELECTROGRAM SIGNALS USING A PATTERN RECOGNITION DEVICE

CROSS REFERENCES TO RELATED APPLICATIONS

This application is a continuation-in-part (CIP) of U.S. patent application Ser. No. 11/416,317, filed May 1, 2006, entitled "System And Method For Detecting Abnormal Respiration Via Respiratory Parameters Derived From Intracardiac Electrogram Signals", which was a CIP of U.S. patent application Ser. No. 11/127,389, filed May 11, 2005, entitled "System and Method for Detection of Respiration Patterns via Intracardiac Electrogram Signals", which claimed the benefit of U.S. Provisional Patent Application Ser. No. 60/631,111, filed Nov. 24, 2004. This application is also related to co-pending U.S. patent application Ser. No. 11/558,787, filed contemporaneously herewith, entitled "System and Method for Detecting Physiologic States Based on Intracardiac Electrogram Signals while Distinguishing Cardiac Rhythm Types". Each of these applications is incorporated by reference herein.

FIELD OF THE INVENTION

The invention generally relates to implantable medical devices, such as pacemakers or implantable cardioverter/defibrillators (ICDs), and in particular, to techniques for detecting respiration patterns within a patient in which a medical device is implanted, including abnormal respiration patterns such as apnea, hypopnea or nocturnal asthma.

BACKGROUND OF THE INVENTION

It is highly desirable to reliably track respiration within patients having pacemakers and ICDs. Tracking patient respiration permits potentially dangerous respiratory disorders, such as apnea, hypopnea, hyperpnea, nocturnal asthma, and Cheyne-Stokes Respiration (CSR), to be detected. Apnea and hypopnea are abnormal respiration patterns characterized by periods of significantly reduced respiration. With hypopnea, respiration is reduced but still present. With apnea, however, respiration may cease completely for 10 seconds or longer. One common form of apnea is central sleep apnea (CSA), which appears to arise during sleep due to a neurological defect. Another form of apnea is obstructive sleep apnea (OSA), which arises due to obstruction of the respiratory pathways during sleep. Patients with sleep apnea experience frequent wakefulness at night and excessive sleepiness during the day. In addition, apnea can exacerbate various medical conditions, particularly hypertension. Apnea can also exacerbate congestive heart failure (CHF), a condition wherein the patient suffers from poor cardiac function. Indeed, the aberrant blood chemistry levels occurring during sleep apnea are a significant problem for patients with CHF. Due to poor cardiac function caused by CHF, patients already suffer from generally low blood oxygen levels. Frequent periods of sleep apnea result in even lower blood oxygen levels.

Episodes of apnea can also occur during CSR, which is an abnormal respiratory pattern often occurring in patients with CHF. CSR is characterized by alternating periods of hypopnea and hyperpnea (i.e. fast, deep breathing.) Briefly, CSR arises principally due to a time lag between blood CO_2 levels sensed by the respiratory control nerve centers of the brain and the blood CO_2 levels. With CHF, poor cardiac function results in poor blood flow to the brain such that respiratory control nerve centers respond to blood CO_2 levels that are no longer properly representative of the overall blood CO_2 levels in the body. Hence, the respiratory control nerve centers trigger an increase in the depth and frequency of breathing in an attempt to compensate for perceived high blood CO_2 levels—although the blood CO_2 levels have already dropped. By the time the respiratory control nerve centers detect the drop in blood CO_2 levels and act to slow respiration, the blood CO_2 levels have already increased. This cycle becomes increasingly unbalanced until respiration alternates between hypopnea and hyperpnea. The periods of hypopnea often become sufficiently severe that no breathing occurs between the periods of hyperpnea, i.e. periods of frank apnea occur between the periods of hyperpnea. The wildly fluctuating blood chemistry levels caused by alternating between hyperpnea and apnea/hypopnea can significantly exacerbate CHF and other medical conditions. When CHF is still mild, CSR usually occurs, if at all, only while the patient is sleeping. When it becomes more severe, CSR can occur while the patient is awake.

Abnormal respiration during sleep may also arise due to nocturnal asthma. With asthma, the linings of the airways swell and become more inflamed. Mucus clogs the airways and the muscles around the airways tighten and narrow. Hence, breathing becomes difficult and stressful. During an asthma attack, rapid breathing patterns similar to hyperpnea occur, though little or no oxygen actual reaches the lungs. An asthma attack may be triggered by allergens, respiratory infections, cold and dry air, or even heartburn. The majority of asthma attacks occur during the night, between 3:00 a.m. and 5:00 a.m. Nocturnal asthma has been associated with factors such as decreased pulmonary function, hypoxemia and circadian variations of histamine, epinephrine, and cortisol concentrations. Asthma attacks at night may also be triggered directly by sleep apnea. Nocturnal asthma attacks may be fatal, particularly within patients also suffering from CHF.

In view of the significant adverse consequences of apnea/hypopnea, nocturnal asthma, or CSR, particularly insofar as patients with CHF are concerned, it is highly desirable to provide techniques for detecting such conditions. Tracking actual patient respiration provides perhaps the most direct and effective technique for detecting respiratory disorders. For patients with pacemakers and ICDs, respiration is conventionally tracked based on thoracic impedance as measured via pacing/sensing leads implanted within the heart. Sensing of the intracardiac electrogram (IEGM) of the patient is temporarily suspended during each cardiac cycle so as to sense an impedance signal, from which respiration patterns are derived. See, for example, U.S. Pat. No. 6,449,509 to Park, et al., entitled "Implantable Stimulation Device Having Synchronous Sampling for a Respiration Sensor."

Although impedance-based techniques are useful, it would be desirable to provide alternative techniques for tracking respiration, particularly for the purposes of detecting episodes of abnormal respiration, wherein respiration is derived solely from the IEGM signal so as to eliminate the need to detect or process impedance. Additionally, this eliminates need for additional sensors, and the sensing electrodes can be thus used for IEGM based breathing pattern detection and hence, the ease of implementability in current platforms. One technique for deriving respiration from an IEGM signal is set forth in U.S. Pat. No. 6,697,672 to Andersson, entitled "Implantable Heart Stimulator", which is incorporated by reference herein. Briefly, Andersson provides a technique to extract parameters related to patient respiration from an analysis of intervals between various events detected within a

ventricular-IEGM (i.e. V-IEGM) signal. For example, cycle-to-cycle variability is tracked in R-R intervals or in the amplitude of S-T intervals. In other words, the technique of Andersson exploits interval-based morphological features of the V-IEGM to track respiration. Although not discussed in the Andersson reference, autonomic variability arising during respiration causes the interval-based changes in the IEGM. R-waves (also referred to as QRS-complexes) are electrical signals representative of the depolarization of ventricular muscle tissue. The subsequent electrical repolarization of the ventricular tissue appears within the IEGM as a T-wave. Electrical depolarization of atrial muscle tissue is manifest as a P-wave. Strictly speaking, P-waves, R-waves and T-waves are features of a surface electrocardiogram (EKG or ECG). For convenience, the terms P-wave, R-wave and T-wave are also used herein (and in the literature) to refer to the corresponding internal signal component.

Although the interval-based variability technique of Andersson is effective, it is desirable to provide additional or alternative IEGM-based techniques for trending and tracking respiration and for detecting episodes of abnormal respiration. This general goal was achieved by the techniques of patent application Ser. No. 11/127,389, cited above. Briefly, respiration patterns are detected based upon cycle-to-cycle changes in morphological features associated with individual electrical events with the IEGM signals. For example, slight changes in the peak amplitudes of QRS-complexes, P-waves or T-waves are tracked to identify cyclical variations representative of patient respiration. Alternatively, the integrals of the morphological features of the individual events may be calculated for use in tracking respiration. Once respiration patterns have been identified, episodes of abnormal respiration, such as apnea, hyperpnea, nocturnal asthma, or the like, may be detected and therapy automatically delivered.

Hence, the techniques of patent application Ser. No. 11/127,389, which are also described herein below, are not limited to analyzing interval-based features of a V-IEGM, as with certain predecessor techniques. Instead, the techniques of the parent application examine changes within individual features of cardiac cycles over time. In this regard, it has been observed that respiration causes slight variations in the size and shape of individual electrical events of the IEGM signals, such as QRS-complexes, and that those changes are correlated with respiration. This differs from changes in intervals (such as R-R intervals), which, as noted, appear to arise due to autonomic variability. In one specific example, changes in the integrals of the QRS-complex derived from a V-IEGM channel signal are examined, alone or in combination with, integrals of P-waves derived from an atrial IEGM (A-IEGM) channel signal. Interval-based parameters, such as variations in A-A, R-R or AV intervals, may be additionally used to aid in tracking respiration but are not required. That predecessor application also presented techniques for detecting episodes of abnormal respiration based on respiration patterns derived from IEGMs, such as episodes of such as apnea, hypopnea, nocturnal asthma, or CSR.

Patent application Ser. No. 11/416,317 provided further improvements in the area of abnormal respiration detection based on IEGM signals. These improvements, which are also described herein below, are particularly directed to exploiting respiratory parameters such as inter-breath interval, respiration depth, and respiration power in the detection of abnormal respiration, with each of the respiratory parameters conveniently derived from IEGM signals. These techniques are particularly well suited to detecting episodes of abnormal respiration during sleep. In this regard, normal respiration during sleep is characterized by an almost constant respiration depth (corrected for patient posture and other non-respiratory factors). Hence, significant changes in respiration depth or other parameters associated with the respiratory cycles are indicative of a transition from normal respiration to some form of abnormal respiration. Further analysis of the respiratory parameters is used to identify the particular form of abnormal respiration. The technique can also be used to track and trend sleep disorder breathing or, in general, disordered breathing. Depending upon the capabilities of the implanted device, appropriate therapy may then be delivered. For example, an alarm device may be triggered to alert the patient upon detection of an episode of apnea/hypopnea. The alarm device may be, e.g., an implanted device such as a "tickle" voltage warning device or a bedside warning system that emits an audible alarm. In this manner, if the patient is asleep, the patient is thereby awakened so as to prevent extended episodes of apnea/hypopnea from occurring, which can cause significant variances in blood chemistry that can exacerbate other medical conditions such as CHF.

Although the techniques of the predecessor applications cited above are quite useful, room for still further improvement remains. In particular, it would be desirable to exploit pattern classifiers (such as pattern classifiers of the type described in U.S. Pat. No. 7,025,729 to de Chazal, et al., entitled "Apparatus for Detecting Sleep Apnea using Electrocardiogram Signals") to discriminate normal and abnormal respiration based on IEGM signals detected by an implantable medical device. It would also be desirable to evaluate the severity of abnormal respiration within a patient and to further discriminate different types of abnormal respiration, such as to discriminate CSA from OSA. Accordingly, various aspects of the present invention are directed to these ends.

SUMMARY

In one embodiment, a method is provided for detecting abnormal respiration within a patient using an implantable medical device. IEGM signals (or other cardiac electrical signals) are sensed within the patient in which the device is implanted. Cardiac cycles (i.e. heartbeats) are identified within the IEGM signals. Then, one or more parameters associated with the cardiac cycles are detected or extracted from the cardiac cycles. Such parameters may include morphology-based metrics such as various integrals, as well as interval-based metrics such P-P, R-R, and P-R intervals. Abnormal respiration is then detected by applying the parameters of the cardiac cycles to a device trained to discriminate between normal and abnormal respiration such as a pattern classifier. In one particular example, the pattern classifier is a 2-class linear discriminant pattern classifier trained to discriminate between normal and apneic/hypopneic respiration. In another example, the pattern classifier is a 3-class pattern classifier trained to further discriminate between CSA and OSA. Additionally, the pattern classifier may be configured to output an indication of the severity of abnormal respiration within the patient. In certain preferred implementations, the pattern classifier is trained to determine whether the patient is subject to apnea/hypopnea but does not specifically identify individual episodes of apnea/hypopnea. Diagnostic data is recorded for physician review, which indicates that the patient is apneic/hypopneic. In other implementations, the pattern classifier is instead trained to identify individual episodes of apnea/hypopnea. If an individual episode of abnormal respiration is detected, the implanted device might then generate warning signals and/or deliver appropriate therapy, as well as recording diagnostic data for subsequent physician review.

In some embodiments, the device further distinguishes among four different cardiac rhythms: AR (paced atrial beats/intrinsic ventricular beats); AV (paced atrial beats/paced ventricular beats); PR (intrinsic atrial beats/intrinsic ventricular beats); and PV (intrinsic atrial beats/paced ventricular beats). That is, the device determines which of the four basic cardiac rhythm types is currently occurring within the patient. The device extracts different morphological and interval-based parameters depending upon the current rhythm type. One of four different pre-trained pattern classifiers is then activated to discriminate normal from abnormal respiration using the extracted parameters. Thus, if the patient is undergoing fully intrinsic (i.e. PR) cardiac rhythms, the pattern classifier specifically trained for use with PR rhythms is used to detect abnormal respiration. If the patient is instead undergoing fully paced (i.e. AV) cardiac rhythms, the pattern classifier specifically trained for use with AV rhythms is instead used to detect abnormal respiration, etc. Alternatively, a single pattern classifier is instead used, which is loaded with different classifier parameters depending upon the current cardiac rhythm. In any case, improved respiratory discrimination can be achieved by taking into account cardiac rhythm type.

Thus, by employing a pattern classifier or other properly trained pattern recognition device or algorithm, improvements in abnormal respiration detection and discrimination can be achieved. These improvements are preferably implemented within implantable medical devices to permit the device itself to detect episodes of abnormal respiration and record appropriate diagnostics. However, principles of the invention are also applicable to external devices when used in conjunction with implanted devices. For example, an external programmer device may be equipped to detect abnormal respiration within a patient based on IEGM data sensed by a device implanted within the patient and sent via telemetry to the programmer for processing.

BRIEF DESCRIPTION OF THE DRAWINGS

The above and further features, advantages and benefits of the invention will be apparent upon consideration of the descriptions herein taken in conjunction with the accompanying drawings, in which:

FIG. **1** illustrates pertinent components of an implantable medical system having a pacer/ICD capable of: tracking respiration patterns based on IEGM signals detected via leads mounted in the heart; detecting episodes of abnormal respiration based on the respiration patterns; and delivering therapy or warning signals in response thereto;

FIG. **2** is a flow chart providing an overview of the method for tracking respiration patterns based on IEGM signals, which may be performed by the system of FIG. **1**;

FIG. **3** is a flow chart specifically illustrating depolarization-based respiration detection techniques, which may be performed by the system of FIG. **1**;

FIG. **4** is a graph illustrating exemplary unipolar IEGM patterns and resulting respiration patterns derived from an analysis of the integrals of QRS complexes generated via the method of FIG. **3**;

FIG. **5** is a graph illustrating exemplary unipolar IEGM patterns (shown superimposed on one another) and resulting respiration patterns derived from an analysis of the integrals of QRS-complexes generated via the method of FIG. **3**;

FIG. **6** is a graph illustrating respiration patterns derived from an analysis of the peak-to-peak amplitudes of P-waves generated via the method of FIG. **3**;

FIG. **7** is a graph illustrating respiration patterns derived from an analysis of the peak-to-peak amplitudes of intrinsic QRS-complexes generated via the method of FIG. **3**;

FIG. **8** is a flow chart specifically illustrating repolarization-based respiration detection techniques, which may be performed by the system of FIG. **1**;

FIG. **9** is a graph illustrating exemplary unipolar ventricle paced IEGM patterns and resulting respiration patterns derived from an analysis of the integrals of T-waves generated via the method of FIG. **8**;

FIG. **10** is a graph illustrating exemplary unipolar intrinsic Ventricular IEGM patterns (shown superimposed on one another) and resulting respiration patterns derived from an analysis of the integrals of T-waves generated via the method of FIG. **8**;

FIG. **11** is a graph illustrating respiration patterns derived from an analysis of the peak-to-peak amplitudes of T-waves generated via the method of FIG. **8**;

FIG. **12** is a graph illustrating respiration patterns derived from an analysis of the maximum amplitudes of T-waves generated via the method of FIG. **8**;

FIG. **13** is a flow chart specifically illustrating interval-based respiration detection techniques, which may be performed by the system of FIG. **1**;

FIG. **14** is a flow chart illustrating abnormal respiration detection techniques, which may be performed by the system of FIG. **1**, based on respiration patterns detecting using the techniques of FIGS. **2-13**;

FIG. **15** is a graph illustrating a sixteen hour respiration pattern derived from an analysis of the maximum amplitudes of T-waves for use in identifying trends for use with the method of FIG. **14**;

FIG. **16** is a simplified, partly cutaway view, illustrating the pacer/ICD of FIG. **1** along with a complete set of leads implanted in the heart of a patient;

FIG. **17** is a functional block diagram of the pacer/ICD of FIG. **16**, illustrating basic circuit elements that provide cardioversion, defibrillation and/or pacing stimulation in four chambers of the heart and particularly illustrating an IEGM-based respiration pattern detector, an IEGM-based abnormal respiration episode detector, and an abnormal respiration therapy controller; and

FIG. **18** is a flow chart providing an overview of improved methods for detecting abnormal respiration patterns, which may be performed in furtherance of the techniques of FIG. **14**;

FIG. **19** is a flow chart illustrating exemplary steps directed to identifying individual respiratory cycles in accordance with the technique of FIG. **18**;

FIG. **20** is a graph illustrating an exemplary cardiac cycle and particularly illustrating historical ranges of values for the T-wave that may used in connection with the techniques of FIG. **19** to extract temporal and morphological parameters;

FIG. **21** is a graph illustrating an exemplary distribution of paced depolarization (PDI) values that may be analyzed via the techniques of FIG. **19** to reject fused beats;

FIG. **22** is a graph illustrating exemplary cardiac cycles and various parameters derived therefrom via the techniques of FIG. **19**, along with externally-derived signals representative of patient respiration for comparison;

FIG. **23** is a flow chart illustrating exemplary steps directed to identifying detecting parameters associated with individual respiratory cycles in accordance with the technique of FIG. **18**;

FIG. **24** is a graph illustrating exemplary respiratory cycle parameters that may be analyzed via the techniques of FIG. **19**, along with externally-derived signals representative of patient respiration for comparison;

FIG. **25** is a flow chart illustrating exemplary steps directed to detecting significant changes in the respiratory parameters in accordance with the technique of FIG. **18**;

FIG. **26** is a flow chart illustrating exemplary steps directed to evaluating the significant changes to detect abnormal respiration in accordance with the technique of FIG. **18**;

FIG. **27** is a flow chart summarizing the overall abnormal respiration detection procedures of FIGS. **18-26**;

FIG. **28** is a flow chart providing an overview of abnormal respiration detection techniques that exploit pattern classifiers, and which may be implemented by implantable devices such as the pacer/ICD of FIG. **1**;

FIG. **29** is a flow chart illustrating a first exemplary technique for detecting abnormal respiration in accordance with the general technique of FIG. **28**, wherein a 3-class pattern classifier is trained to discriminate among normal respiration, CSA and OSA;

FIG. **30** is a flow chart further illustrating the first exemplary technique of FIG. **29**, wherein the 3-class pattern classifier, once trained, is then activated to discriminate among normal respiration, CSA and OSA within the patient;

FIG. **31** is a graph illustrating the use of the pattern classifier techniques of FIG. **30** while the patient is asleep to detect various forms of sleep apnea;

FIG. **32** is a flow chart providing a more detailed illustration of the technique of FIG. **30**, particularly showing the use of one-minute long epochs for detecting abnormal respiration;

FIG. **33** is a flow chart illustrating a second exemplary technique for detecting abnormal respiration in accordance with the general technique of FIG. **28**, wherein separate pattern classifiers are trained based on different cardiac rhythm types;

FIG. **34** is a flow chart further illustrating the second exemplary technique of FIG. **33**, wherein different parameters are extracted from the IEGM signals of the patient based on the current cardiac rhythm type for use with a corresponding pattern classifier; and

FIG. **35** is a functional block diagram of an alternative implementation of the pacer/ICD of FIG. **16**, illustrating basic circuit elements that provide cardioversion, defibrillation and/or pacing stimulation in four chambers of the heart and particularly illustrating pattern classification-based components for use in discriminating normal and abnormal respiration.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The following description includes the best mode presently contemplated for practicing the invention. This description is not to be taken in a limiting sense but is made merely to describe general principles of the invention. The scope of the invention should be ascertained with reference to the issued claims. In the description of the invention that follows, like numerals or reference designators are used to refer to like parts or elements throughout.

Overview of Implantable Medical System

FIG. **1** illustrates an implantable medical system **8** having a pacer/ICD capable of tracking respiration based on IEGM signals, identifying episodes of abnormal respiration and delivering appropriate therapy. To this end, pacer/ICD **10** receives voltage signals from various cardiac pacing leads (only two of which are shown in the FIG. **1**) from which various channels of IEGM signals are derived including, for example, unipolar or bipolar A-IEGM signals and unipolar or bipolar V-IEGM signals. A complete set of exemplary pacing leads are shown in FIG. **16** from which a wide variety of specific channels of IEGM signals may be derived. Based on the IEGM signals, the pacer/ICD detects parameters associated with patient respiration using a technique broadly summarized below with reference to FIG. **2**. Examples that are more specific are set forth in FIGS. **3-13**. Based on the respiration parameters, the pacer/ICD then also detects individual episodes of abnormal respiration, such as apnea, asthma or CSR.

Once an episode of abnormal respiration has been detected, the pacer/ICD uses additional implanted components (if so equipped) to deliver appropriate therapy or warning signals. For example, if apnea/hypopnea is detected, the pacer/ICD may activate an internal alarm **18** or an external bedside alarm **22**. Internal alarm **18** may be a vibrating device or a "tickle" voltage device that, in either case, provides perceptible stimulation to the patient to alert or awaken the patient so as to terminate the episode of apnea/hypopnea. The bedside alarm may provide audible or visual alarm signals of sufficient magnitude to alert or awaken the patient. If an activity sensor is provided within the pacer/ICD, the form of the alarm may be controlled based on patient activity. For example, if the activity level indicates that the patient is asleep, a more noticeable alarm may be employed than if the patient is deemed to be awake. In addition, while the patient is asleep, the intensity of the alarm signal can be periodically increased until the patient awakens, as detected by the activity sensor. Additionally, or in the alternative, the system may include a drug pump **20** capable of the delivering medications in an attempt to prevent the onset of additional episodes of apnea/hypopnea. Discussions of exemplary medications are provided below. In addition, the pacer/ICD may deliver atrial overdrive pacing for the purposes of preventing additional episodes of apnea/hypopnea from occurring.

Thus, FIG. **1** provides an overview of an implantable system for tracking respiration, detecting episodes of abnormal respiration and for delivering therapy in response thereto. Although a pacer/ICD is illustrated in FIG. **1**, it should be understood that the detection techniques of the invention may be implemented within other implantable devices, including dedicated respiration detection devices not necessarily capable of providing cardiac stimulation therapy. Note also that internal signal transmission lines for interconnecting the various implanted components are not shown. Alternatively, wireless signal transmission may be employed. In addition, it should be appreciated that systems provided in accordance with invention need not include all the components shown in FIG. **1**. In many cases, for example, the system will include only the pacer/ICD and its leads. Other implementations will employ internal or external alarms but no drug pumps. These are just a few exemplary embodiments. No attempt is made herein to describe all possible combinations of components that may be provided in accordance with the general principles of the invention. Also, note that the particular locations of the implanted components are merely exemplary.

Overview of Technique for Tracking Respiration Using IEGM

FIG. **2** provides an overview of the techniques of the invention for tracking respiration patterns via morphological features of IEGM signals. Initially, at step **100**, IEGM signals are sensed by an implantable medical device, such as the pacer/ICD of FIG. **1**. As will be explained in greater detail with reference to the specific examples below, the IEGM signals may be atrial channel signals, ventricular channel signals, cross chamber signals, or some combination thereof. In any

case, at step **102**, individual cardiac cycles are identified within the IEGM signals using otherwise conventional detection techniques, which typically operate to detect cardiac cycles based on QRS-complexes. At step **104**, selected electrical events are identified within the IEGM signals, such as depolarization events (e.g. QRS-complexes or P-waves) or repolarization events (i.e. T-waves). At step **106**, morphological parameters associated with the individual events are detected—such as the maximum amplitude of the event, the peak-to-peak amplitude of the event, or the numerical integral of the event (i.e. the total energy associated with the event). As will be explained, multiple parameters may be detected for each individual event (e.g. both the maximum amplitude and integral of an event may be detected) and different parameters may be detected for different events (e.g. the peak-to-peak amplitude may be determined for P-waves whereas an integral may be calculated for T-waves.)

Then, at step **108**, patient respiration is detected based on cycle-to-cycle changes in the morphological parameters (such as cycle-to-cycle variations in the integral of the QRS-complexes or cycle-to-cycle changes in the maximum amplitudes of P-waves). In other words, changes in morphology of a given parameter from one beat to another are tracked for the purposes of detecting respiration patterns. This differs from changes in intervals (such as R-R intervals), which, as noted above, appear to arise due to autonomic variability.

The slight variations in the morphology of individual events within the IEGM are tracked from cycle-to-cycle so as to detect the cyclical changes associated with normal respiration. Otherwise conventional filters may be used to isolate cyclical patterns appearing at frequencies associated with respiration. Additionally, an analysis of changes in the intervals between beats may be used to enhance the reliability of the respiration detection technique of step **108**. In particular, the techniques described in the above-referenced patent to Andersson may be employed. Variability in AV or A-A intervals may also be employed. In other words, both interval-based and individual feature-based techniques may be employed to enhance detection specificity.

Depolarization-Based Respiration Detection Examples

Turning now to the FIGS. **3-7**, examples of the technique specifically directed to the use of depolarization-based parameters (i.e. P-waves and QRS-complexes) will now be described. Beginning at steps **200** and **202**, the pacer/ICD (or other implanted medical device) senses A-IEGM and V-IEGM channel signals. The signals may be derived from a lead configuration that may be unipolar, bipolar or cross-chamber (i.e. signals sensed between electrodes is separate chambers such as between A-tip to V-tip.) The specific channel used may be right atrium, right/left Ventricle. Far field QRS or T-waves can be analyzed in the atrial channel i.e. far-field R-waves and ventricular repolarization (T-waves). Additionally, the Ventricular channel near-field QRS and T-waves can be used. In any case, at step **204**, selected depolarization-based features are detected within the IEGM signals. Examples include P-waves, QRS-complexes, atrial evoked responses (AERs) and ventricular evoked responses (VERs). Different features may be detected within different IEGM channel signals. For example, P-waves and AERs may be detected within A-IEGM channel signals; whereas QRS-complexes and VERs may be detected within V-IEGM channel signals. At step **206**, the pacer/ICD calculates the numerical integral, the maximum amplitude and/or the peak-to-peak amplitude of the detected features or other suitable morphological parameters. Maximum or peak amplitude of an event represents the maximum of the absolute value of the respective IEGM channel signal during the event. Peak-to-peak amplitude instead represents the difference between the highest and lowest values of the respective IEGM channel signal during the event. With a baseline voltage of zero, the peak-to-peak amplitude thereby represents the difference between the largest positive and largest negative values of the IEGM signal during the event. Insofar as integrals of paced events are concerned, a paced depolarization integral (PDI) is preferably calculated. Otherwise conventional techniques for calculating PDIs may be employed. See, for example, U.S. Pat. No. 6,731,985 to Poore, et al., entitled "Implantable Cardiac Stimulation System and Method for Automatic Capture Verification Calibration.") For paced beats, the PDI is more useful than QRS amplitude because the PDI provides an improved the signal-to-noise ratio. In any case, at step **208**, the pacer/ICD tracks changes in the calculated parameters from cycle-to-cycle (typically over at least a few dozen cardiac cycles) and, at step **210**, derives respiration parameters from those changes.

Specific examples are illustrated in FIGS. **4-7**. Within FIG. **4**, a first graph **212** illustrates a unipolar V-IEGM signal for a canine test subject paced at 90 beats per minute (bpm). The vertical axis of the graph illustrates the output of an analog-to-digital converter (ADC) applied to the unipolar IEGM signal. The output ADC count is represented on arbitrary numerical scale (scaled to have only positive values), which is generally representative of the voltage associated with the unipolar IEGM signals, scaled so that all values are positive. FIG. **4** shows the IEGM signals associated with a plurality of cardiac cycles superimposed one upon the other so as to particularly illustrating slight variations in the shape of the patterns from cycle-to-cycle. The horizontal axis represents time within the individual cardiac cycles in milliseconds from a common starting point. A second graph, **214**, illustrates the integrals of the VERs associated with each ventricular pacing pulse. In other words, the VER within each individual cardiac cycle of graph **212** was numerically integrated to obtain a single value, then those values were plotted as a function of time to produce graph **214**. (The integrals of VERs are also referred to as PDIs.) Within graph **214**, the vertical axis represents the integral value in arbitrary numerical units. The vertical horizontal axis represents time in seconds.

The integrals from the VERs of graph **212** have been connected by an interpolated line so as to provide a smooth representation of the respiration pattern of the canine test subject. More complex methods may be used to interpolate by using curve fitting of functions or by using a reconstruction filter. When a patient is awake/active, curve fitting can instead be used to provide smooth representation to calculate the breathing rate. As can be seen, there is clearly a cyclical pattern composed of alternating peaks and nadirs, from which respiration information may be derived. In particular, the rate of respiration may be derived (using otherwise conventional signal processing and analysis techniques) based upon the interval from one peak to another or the interval from one nadir to another. The relative amplitude of respiration may be derived based on comparison of the amplitude of the respective peaks and nadir of a given respiration cycle. Hence, although the respiration pattern of graph **214** does not necessarily closely represent an actual canine respiration pattern (which is typically more sinusoidal, particularly during fairly fast-paced respiration), the respiration pattern of graph **214** is nevertheless sufficient to obtain gross information pertaining to respiration, such as rate and relative amplitude from which episodes of abnormal respiration may be detected.

A second depolarization-based example is shown in FIG. **5**, again for a canine test subject (although in this case, using

intrinsic beats rather than paced beats). A first graph **216** illustrates QRS-complexes (as well as T-waves) derived from a unipolar ventricular lead. The IEGM signals associated with a plurality of cardiac cycles are superimposed one upon the other. Again, the vertical axis illustrates voltage in terms of an ADC count. The horizontal axis represents time within the individual cardiac cycles in milliseconds from a common starting point. The graph **218** shows a resulting, smoothed respiration pattern derived by integrating the QRS complexes shown in graph **216**. Again, a cyclical pattern appears, which is representative of the respiration of the canine test subject. Gross information pertaining to respiration may be derived, including respiration rate and relative amplitude.

Another depolarization-based example is shown in FIG. **6**, this one based on P-wave maximum (or peak) amplitude. In FIG. **6**, only the resulting respiration pattern is shown (by way of graph **220**), not the P-waves themselves. The vertical axis represents peak amplitude on an arbitrary voltage scale; whereas the horizontal axis illustrates time in seconds. The data was derived from a canine test subject based on atrial unipolar IEGM channel signals. The peak amplitude of each P-wave within each cardiac cycle was detected and the resulting plot of P-wave amplitude as a function of beat number smoothed. As with the other plots, a cyclical pattern is apparent, which is representative of respiration. A final depolarization-based example is shown in FIG. **7**, which illustrates a respiration pattern (via graph **222**) derived from QRS-complex maximum amplitudes sensed via a unipolar ventricular lead for a canine test subject. The maximum or peak amplitude of the QRS-complex of each cardiac cycle was detected, plotted along a time axis, and the resulting graph smoothed. Again, the gross features of the canine respiration pattern are clearly evident.

Thus, FIGS. **4-7** illustrate various examples of respiration patterns derived by separately plotting various depolarization-based features of IEGM signals. It is possible to also use two or more separate parameters to track respiration to improve accuracy. For example, respiration plots may be generated based upon QRS complexes derived separately from different channels, with the separate plots then merged to yield a single respiration plot (using, for example, otherwise conventional interpolation techniques). Alternatively, respiration patterns derived from different parameters, such as one from QRS-complexes and one from P-waves may be merged and combined to form a smooth time domain interpolation of breathing pattern. Additional morphological parameters, such as the peak slope of an event, might be suitable as well. Otherwise routine experimentation may be performed to determine which additional parameters might be suitable for tracking respiration and to identify the optimal combinations of various parameters to be combined so as to most reliably track patient respiration.

Repolarization-Based Respiration Detection Examples

Turning now to the FIGS. **8-12**, examples specifically directed to the use of repolarization-based parameters (i.e. T-waves) will now be described. Many of the features of these techniques are similar to the depolarization-based techniques already described and so only pertinent differences will be described. Beginning at step **300** of FIG. **8**, the pacer/ICD senses V-IEGM signals (or senses cross-chamber signals having strong ventricular components.) At step **302**, a repolarization-based feature is detected within the IEGM signals, typically the ventricular T-wave. Potentially, atrial repolarization events may also be detected and used to track respiration. However, atrial repolarization events are typically of low amplitude and difficult to detect and thus are not optimal for use in tracking respiration. Hence, the use of atrial repolarization events will not be described in any great detail herein.) At step **304**, the pacer/ICD calculates the numerical integral, the maximum amplitude and/or the peak-to-peak amplitude of the detected T-waves. At step **306**, the pacer/ICD tracks changes in the calculated T-wave parameters from cycle-to-cycle and, at step **308**, derives respiration based on changes in the T-waves. In this regard, far-field ventricular depolarization events as detected in the atrium can be used to aid in tracking repolarization.

Specific T-wave-based examples are illustrated in FIGS. **9-12** for a canine test subject. Within FIG. **9**, graph **312** illustrates a unipolar V-IEGM signal for a canine test subject paced at 90 bpm. FIG. **9** shows the IEGM signals associated with a plurality of cardiac cycles superimposed one upon the other. The horizontal axis represents time within the individual cardiac cycles in milliseconds from a common starting point. Graph **314** illustrates the integrals of the T-waves from cycle-to-cycle. The individual data points derived by integrating the T-waves of graph **312** have been interpolated so as to provide a smooth representation of the respiration pattern of the canine test subject. A cyclical pattern appears, from which respiration information may be derived. Although the respiration pattern of graph **314** does not closely represent an actual respiration pattern, graph **314** is nevertheless sufficient to obtain gross information pertaining to patient respiration, such as rate, depth and effort.

A second repolarization-based example is shown in FIG. **10**, again for a canine test subject (although in this case, using intrinsic beats rather than paced beats). A first graph **316** illustrates T-waves (as well as QRS-complexes) derived from a unipolar ventricular lead, with the T-waves superimposed one upon the other. Graph **318** shows the resulting, interpolated respiration pattern derived by integrating the T-waves. Again, a cyclical pattern appears, representative of the respiration of a canine test subject from which gross information pertaining to respiration may be derived, including respiration rate and relative amplitude.

Another repolarization-based example is shown in FIG. **11**, this one based on T-wave maximum amplitude. In FIG. **11**, only the resulting respiration pattern shown (by way of graph **320**), not be the T-waves themselves. The peak amplitude of each T-wave within each cardiac cycle was detected and the resulting plot of T-wave amplitude as a function of beat number is smoothed. As with the other plots, a clearly cyclical pattern appears, representative of respiration. A final repolarization-based example is shown in FIG. **12**, which illustrates a respiration pattern (via graph **322**) derived from T-wave maximum amplitudes. The maximum amplitude of the T-wave of each cardiac cycle was detected, plotted along a time axis, and the resulting graph smoothed. Again, the gross features of the respiration pattern of the canine test subject are clearly evident.

Thus, FIGS. **8-12** illustrate various examples of respiration patterns derived by separately plotting various repolarization-based features of IEGM signals. It is possible to also use two or more separate T-wave parameters to track respiration, such as both maximum amplitude and peak-to-peak amplitude. Alternatively, respiration patterns derived from different events, such as one from QRS-complexes and one from T-waves may be merged. Using multiple parameters or multiple IEGM channel signals may enhance the specificity with which respiration may be tracked. Otherwise routine experimentation may be performed to determine optimal combinations of the parameters to be combined so as to most reliably track patient respiration.

Interval-Based Respiration Detection Examples

In addition to the aforementioned beat-by-beat tracking techniques, which seek to track respiration based on changes in morphology, intervals between successive beats (or between successive features of an individual beat) may additionally, or alternatively, be employed. This is summarized in FIG. **13**. Beginning at steps **400** and **402**, the pacer/ICD senses A-IEGM and V-IEGM signals. At step **404**, pacer/ICD then detects sequences of consecutive P-waves and/or R-waves within the IEGM signals. At step **406**, selected intervals are calculated, e.g., A-A intervals, AV intervals or R-R intervals. A-A intervals, which represent the intervals between consecutive P-waves, are preferably derived from A-IEGM signals; whereas R-R intervals, which represent the intervals between consecutive QRS-complexes, are preferably derived from V-IEGM signals. Typically, a pacer/ICD calculates these intervals as part of its routine operations. In any case, at step **408**, the pacer/ICD then tracks changes in the intervals from cycle-to-cycle and, at step **410**, derives respiration from changes in the intervals over time, typically, over at least a few dozen cardiac cycles. For example, a given interval value, such as an A-A interval derived from an A-IEGM signals, may be calculated between each successive pair of P-waves, with the value of the interval then plotted as a function of time or as a function of cardiac cycle number (as in some of the examples described above) so as to track the cyclical features of respiration. As before, the respiration patterns derived in this manner may not closely approximate the actual smooth respiration patterns of patient, but nevertheless provide sufficient information from which respiration rate and relative amplitude can be derived and from which episodes of abnormal respiration may be detected.

The use of changes in R-R and ST intervals derived from V-IEGM signals are described in detail with reference to the Andersson cited above. The technique of FIG. **13**, however, is not limited to R-R/ST interval variability derived from V-IEGM signals but, as noted, may be based on either A-IEGM or V-IEGM signals, and may further be based on A-A intervals or AV intervals, or some combination thereof. Unipolar or Bipolar signals may be employed, as well as cross-chamber signals. The respiration patterns derived from cycle-to-cycle changes in intervals may be merged with respiration patterns derived from depolarization events or repolarization events, described above, to provide further specificity.

Abnormal Respiration Detection and Therapy

What have been described thus far are various techniques for tracking respiration patterns based on features of IEGM signals. With reference to FIG. **14**, techniques for detecting episodes of abnormal respiration based on the respiration patterns and delivering therapy will now be described. At step **450**, the pacer/ICD analyzes the detected respiration pattern to detect episodes of abnormal respiration such as apnea and hypopnea, hyperpnea, nocturnal asthma, and CSR, based on respiration rate and/or amplitude. In general, otherwise conventional techniques for detecting episodes of abnormal respiration, which use respiration rates or respiration amplitudes, may be employed. Preferably, however, the techniques set forth in FIGS. **18-27** are employed to detect abnormal respiration. These techniques are described below. Once an episode of abnormal respiration is detected, otherwise conventional techniques may be used to identify the particular form of abnormal respiration, i.e. to distinguish between apnea, hypopnea, hyperpnea, CSR, etc.

Briefly, apnea may be detected based upon a lack of any significant amplitude variations within the detected respiration patterns extending over a predetermined period of time. In one example, an apnea detection amplitude threshold value may be specified along with an apnea detection time threshold value. If the respiratory amplitude derived from the respiration patterns does not exceed the amplitude threshold value for at least a period of time greater than the time threshold value, then apnea is presumed. Typically, an episode of apnea is not deemed to have occurred unless there is a lack respiration for at least ten seconds and so a time threshold of at least ten seconds may be employed. A suitable amplitude threshold value may be determined via routine experimentation for use with respiration patterns derived from particular IEGM parameters. In this regard, the amplitude threshold value for use with the respiration patterns derived from QRS-complexes may differ from one derived from the P-waves or T-waves. The values may also differ from patient to patient. Note that the amplitude and morphology changes may also depend on body position, and also on the rhythm types, i.e. in case of a pacer/ICD, it would be advisable to have different thresholds for different rhythm combinations: A-R, A-V, P-R, P-V. Suitable amplitude threshold values may be specified following implant of device based on the specific characteristics of patient in which the device is implanted or automatically updated during routine working of the algorithm.

More complex techniques may be employed identifying each episode of apnea. In one example, a combination of raw respiration parameters generated above and various thresholds on each parameter are fed into an apnea episode detection system, specifically configured for detecting apnea. Additionally, simple or more complex methods than zero crossings can be used to determine breathing rate. Depth of breathing and effort of breathing can be calculated. The local variability in each parameter as derived from mean and standdeviations etc. may also be fed as variables into the apnea episode detection system. (Other variables that can be derived include median, peak-to-peak changes, and inter-quartile range.) Using the long term autonomic interval-based variability as well as the individual event-based morphological variability, it is possible to detect differences between obstructive apnea, central apnea, nocturnal apnea, CSA and flow hypopnea etc.

Hypopnea may be detected based upon respiratory amplitude that exceeds the apnea threshold but falls below a separate hypopnea amplitude threshold. As with apnea, a time threshold value (such as 10 seconds) may be specified as well. Hence, if there is at least some respiration, but the amplitude of that respiration falls below an amount deemed healthy for the patient, hypopnea is presumed. As with the various apnea thresholds, separate hypopnea threshold values may be specified for use with different respiration detection techniques (i.e. depolarization-based techniques versus repolarization-based techniques) and for use with different patients, preferably determined on a patient by patient basis following implant of the device. Alternative and more complex hypopnea detection techniques may be employed as well.

Hyperpnea/asthma may be detected based upon a pattern exhibiting excessively rapid respiration (or attempted respiration.) Accordingly, an hyperpnea/asthma amplitude detection threshold may be specified along with a hyperpnea/asthma respiration rate and effort threshold. If amplitude derived from the respiration pattern exceeds the hyperpnea/asthma respiration amplitude detection threshold while the respiration rate (also derived from the respiration pattern) also exceeds it respective threshold, hyperpnea/asthma is thereby presumed. Again, suitable thresholds may be determined on the patient basis following implant of device. Alter-

native and more complex hyperpnea/asthma or CSR detection techniques may be employed as well.

Hyperpnea usually may be distinguished from asthma based on the presence or absence of normal respiration preceding the attack. Hyperpnea usually follows an episode of apnea/hypopnea; whereas asthma usually follows a period of otherwise normal breathing. Episodes of nocturnal asthma may be distinguished from other asthma attacks merely by determining whether the patient is asleep, using otherwise conventional sleep detection techniques. Examples of sleep detection techniques are set forth in: U.S. Pat. No. 5,476,483, to Bornzin et al., entitled "System and Method for Modulating the Base Rate During Sleep for a Rate-responsive Cardiac Pacemaker" and U.S. Pat. No. 6,128,534 to Park et al., entitled "Implantable Cardiac Stimulation Device And Method For Varying Pacing Parameters To Mimic Circadian Cycles."

CSR may be detected using otherwise conventional techniques based on its characteristic pattern of alternating periods of apnea/hypopnea and hyperpnea. See, e.g., U.S. Pat. No. 6,830,548 to Bonnet, et al., "Active Medical Device Able to Diagnose a Patient Respiratory Profile."

Once an episode of abnormal respiration has been detected then, at step **452**, the pacer/ICD delivers appropriate therapy (assuming it is properly equipped). For example, in response to detection of frequent episodes of apnea/hypopnea, atrial overdrive pacing therapy may be applied in an attempt to prevent the onset of additional episodes. A particularly effective atrial overdrive pacing technique, referred to herein as dynamic atrial overdrive (DAO) pacing, is described in U.S. Pat. No. 6,519,493 to Florio et al., entitled "Methods and Apparatus for Overdrive Pacing Heart Tissue Using an Implantable Cardiac Stimulation Device". Routine experimentation may be performed to identify optimal DAO pacing parameters for use with patients with apnea/hypopnea. The aggressiveness of DAO therapy may be adjusted based upon the frequency or duration of episodes of apnea/hypopnea.

Anti-apneic medications may be delivered via an implantable drug pump, if so equipped. Examples of medications that may be helpful in patients with apnea are set forth the following patents: U.S. Pat. No. 6,331,536 to Radulovacki, et al., entitled "Pharmacological Treatment for Sleep Apnea"; U.S. Pat. No. 6,432,956 to Dement, et al., entitled "Method for Treatment of Sleep Apneas"; U.S. Pat. No. 6,586,478 to Ackman, et al., entitled "Methods and Compositions for Improving Sleep"; and U.S. Pat. No. 6,525,073 to Mendel, et al., entitled "Prevention or Treatment of Insomnia with a Neurokinin-1 Receptor Antagonist". Depending upon the particular medication, alternative compounds may be required for use in connection with an implantable drug pump. Routine experimentation may be employed to identify medications for treatment of sleep apnea that are safe and effective for use in connection with an implantable drug pump. Dosages may be titrated based upon the frequency or duration of episodes of apnea.

During the actual episode of apnea/hypopnea, an implantable alarm (such as alarm **18** of FIG. **1**) may be activated to awaken the patient (assuming the patient is sleeping) in an attempt to terminate the episode of apnea/hypopnea. Alternatively, a bedside alarm may be activated by transmission of appropriate wireless control signals. Activation of an alarm to awaken the patient is preferably employed only if other therapy is found to be ineffective, since awakening the patient interrupts with the patient's natural sleeping patterns.

If implantable phrenic nerve stimulators are implanted, apnea/hypopnea therapy can also involve delivery of rhythmic electrical stimulation to the phrenic nerves to mimic breathing (assuming the apnea/hypopnea is due to a lack of phrenic nerve signals.) Examples of phrenic nerve stimulators are set forth in U.S. Pat. No. 5,056,519 to Vince, entitled "Unilateral Diaphragmatic Pacer" and in U.S. Pat. No. 6,415,183 to Scheiner, et al., entitled "Method and Apparatus for Diaphragmatic Pacing", which are incorporated by reference herein. Other respiratory nerves may be stimulated as well. U.S. Pat. No. 5,911,218 to DiMarco, entitled "Method and Apparatus for Electrical Stimulation of the Respiratory Muscles to Achieve Artificial Ventilation in a Patient" describes stimulation of nerves leading to intercostal muscles.

If an implantable hypoglossyl nerve stimulator is implanted, therapy can also involve delivery of stimulation to the hypoglossyl nerves in response to obstructive sleep apnea. Examples of hypoglossyl nerve stimulators are set forth in U.S. Patent Application 2003/0216789 of Deem et al., entitled "Method and System for Treating Sleep Apnea."

Insofar as CSR therapy is concerned, CSR often arises due to CHF and so CSR can often be remedied by addressing the underlying CHF. See, e.g. U.S. patent application Ser. No. 10/792,305, filed Mar. 2, 2004, entitled "System And Method For Diagnosing And Tracking Congestive Heart Failure Based On The Periodicity Of Cheyne-Stokes Respiration Using An Implantable Medical Device". Accordingly, upon detection of episodes CSR, the pacer/ICD preferably employs otherwise conventional techniques to detect CHF and, if CHF is present, any of a variety of therapies directed to mitigating CHF may be implemented by the device. For example, cardiac resynchronization therapy (CRT) may be performed to improve cardiac function. CRT and related therapies are discussed in, for example, U.S. Pat. No. 6,643,546 to Mathis, et al., entitled "Multi-Electrode Apparatus And Method For Treatment Of Congestive Heart Failure"; U.S. Pat. No. 6,628,988 to Kramer, et al., entitled "Apparatus And Method For Reversal Of Myocardial Remodeling With Electrical Stimulation"; and U.S. Pat. No. 6,512,952 to Stahmann, et al., entitled "Method And Apparatus For Maintaining Synchronized Pacing". CHF therapy may also include delivery of medications via an implantable drug pump, if so equipped. Exemplary CHF medications include ACE inhibitors, diuretics, digitalis and compounds such as captopril, enalapril, lisinopril and quinapril. Depending upon the particular medication, alternative compounds may be required for use in connection with an implantable drug pump. Routine experimentation may be employed to identify medications for treatment of CHF that are safe and effective for use in connection with an implantable drug pump.

Additionally, during an individual episode of CSR, the implantable alarm or external bedside alarm may be triggered to awaken the patient to break the cycle of CSR. Again, activation of an alarm to awaken the patient is preferably employed only if other forms of therapy are found to be ineffective. See, also, U.S. patent application Ser. No. 10/844,023, filed May 11, 2004, entitled "System and Method for Providing Demand-Based Cheyne-Stokes Respiration Therapy Using an Implantable Medical Device".

Insofar as hyperpnea is concerned, hyperpnea may arise during CSR or may arise during an asthma attack. Hyperpnea arising due to CSR is preferably addressed via CSR therapy. See, also, U.S. patent application Ser. No. 10/829,719, filed Apr. 21, 2004, entitled "System and Method for Applying Therapy during Hyperpnea Phase of Periodic Breathing Using an Implantable Medical Device". Hyperpnea arising due to asthma may be addressed by addressing the asthma via suitable medications delivered via the implantable drug pump. Examples of asthma medications are set forth, for

example, in U.S. Pat. No. 4,089,959 to Diamond, entitled "Long-Acting Xanthine Bronchodilators and Antiallergy Agents". Depending upon the particular medication, alternative compounds may be required for use in connection with an implantable drug pump. Routine experimentation may be employed to identify medications for treatment of asthma that are safe and effective for use in connection with an implantable drug pump. Dosages may be titrated as needed based on tracking and trending of such breathing patterns.

Additional techniques may be used, if desired, to corroborate the detection of an episode of abnormal respiration made using the techniques of the invention before therapy is delivered. See, e.g., U.S. patent application Ser. No. 10/883,857, filed Jun. 30, 2004, entitled "System And Method For Real-Time Apnea/Hypopnea Detection Using An Implantable Medical System and U.S. patent application Ser. No. 10/821,241, filed Apr. 7, 2004, entitled "System And Method For Apnea Detection Using Blood Pressure Detected via an Implantable Medical System".

Continuing with FIG. **14**, at step **454**, suitable warning signals may be delivered to alert the patient, his/her physician or other medical personnel to any episodes of abnormal breathing.

At step **456**, the device also tracks and trends changes in respiration patterns. This may be achieved by continuously monitoring the patient for apneic or hypopneic events and quantifying the amount of apnea based on an index. A commonly used index is the apnea hypopnea index (AHI). This index is based on counting apnea and hypopneas that occur over the entire night and dividing the number of apnea and hypopneas by the total sleep time in hours. This invention provides a surrogate for AHI using the number of IEGM detected apneas and hypopneas divided by the total rest time in hours. The total rest time approximates the total sleep time and is derived measuring the time that a patient is at profound rest by using an activity sensor as set forth in: in aforementioned patent to Bornzin et al. (U.S. Pat. No. 5,476,483.) Alternatively, the total sleep time may be estimated using IEGM based respiratory rate trends. During sleep, the respiration rate diminishes below the wakeful respiration rates and sleep time may be easily determined using the IEGM based breathing rate trend. In fact, by making a histogram of the IEGM breathing rates sampled at equal intervals throughout the day and counting the number of intervals in the lowest mode an estimate of the duration of sleep may be performed. Another method that may be used to estimate the total sleep time throughout the day depends on a direct current (DC) accelerometer to quantify the amount of time that a patient is lying down as set forth in U.S. Pat. No. 6,466,821, to Pianca et al., entitled "AC/DC Multi-Axis Accelerometer for Determining Patient Activity and Body Position". It is also be possible to use Heart rate dynamics to differentiate between awake and sleep state. See, Redmond et al., "Cardiorespiratory-based sleep staging in subjects with obstructive sleep apnea," IEEE Trans Biomed Eng 2005; 53(3):485-96.

An exemplary trend pattern is illustrated in FIG. **15**, which provides an exemplary breathing pattern (in terms of breathes per minute) tracked over a period of about sixteen hours. A portion **458** illustrate respiration rate during sleep. By analyzing trends contained in breathing patterns such as that of FIG. **15**, the aforementioned surrogate AHI value can be obtained.

Returning to FIG. **14**, appropriate diagnostic information is stored at step **460** so that a medical professional can subsequently review the trend data or any therapy delivered and evaluate its effectiveness.

What have been described are various techniques for tracking respiration via IEGM signals, detecting episodes of abnormal respiration and delivering appropriate therapy. For the sake of completeness, a detailed description of an exemplary pacer/ICD for controlling these functions will now be provided. However, principles of invention may be implemented within other pacer/ICD implementations or within other devices. In particular, techniques of the invention are also applicable to detecting respiration via surface EKG signals and hence are not necessarily limited to use with implantable devices. In this regard, it is known that the mean cardiac axis and EKG morphology is influenced by electrode motion relative to the heart and by changes in thoracic electrical impedance as the lungs fill and empty. The sinus rate is modulated by vagal influences in synchronization with respiration. Pressure changes (i.e. breathing-related as well as cardiac cycle-related pressure changes) influence IEGM morphology.

Exemplary Pacemaker/ICD

FIG. **16** provides a simplified block diagram of the pacer/ICD, which is a multi-chamber stimulation device capable of treating both fast and slow arrhythmias with stimulation therapy, including cardioversion, defibrillation, and pacing stimulation (as well as capable of tracking respiration, detecting episodes of abnormal respiration and delivering appropriate therapy.) To provide atrial chamber pacing stimulation and sensing, pacer/ICD **10** is shown in electrical communication with a heart **612** by way of a left atrial lead **620** having an atrial tip electrode **622** and an atrial ring electrode **623** implanted in the atrial appendage. Pacer/ICD **10** is also in electrical communication with the heart by way of a right ventricular lead **630** having, in this embodiment, a ventricular tip electrode **632**, a right ventricular ring electrode **634**, a right ventricular (RV) coil electrode **636**, and a superior vena cava (SVC) coil electrode **638**. Typically, the right ventricular lead **630** is transvenously inserted into the heart so as to place the RV coil electrode **636** in the right ventricular apex, and the SVC coil electrode **638** in the superior vena cava. Accordingly, the right ventricular lead is capable of receiving cardiac signals, and delivering stimulation in the form of pacing and shock therapy to the right ventricle.

To sense left atrial and ventricular cardiac signals and to provide left chamber pacing therapy, pacer/ICD **10** is coupled to a "coronary sinus" lead **624** designed for placement in the "coronary sinus region" via the coronary sinus os for positioning a distal electrode adjacent to the left ventricle and/or additional electrode(s) adjacent to the left atrium. As used herein, the phrase "coronary sinus region" refers to the vasculature of the left ventricle, including any portion of the coronary sinus, great cardiac vein, left marginal vein, left posterior ventricular vein, middle cardiac vein, and/or small cardiac vein or any other cardiac vein accessible by the coronary sinus. Accordingly, an exemplary coronary sinus lead **624** is designed to receive atrial and ventricular cardiac signals and to deliver left ventricular pacing therapy using at least a left ventricular tip electrode **626**, left atrial pacing therapy using at least a left atrial ring electrode **627**, and shocking therapy using at least a left atrial coil electrode **628**. With this configuration, biventricular pacing can be performed. Although only three leads are shown in FIG. **16**, it should also be understood that additional stimulation leads (with one or more pacing, sensing and/or shocking electrodes) may be used in order to efficiently and effectively provide pacing stimulation to the left side of the heart or atrial cardioversion and/or defibrillation. The leads are also

employed for sensing ID tag signals from medications equipped with active ID transmitters.

A simplified block diagram of internal components of pacer/ICD **10** is shown in FIG. **16**. While a particular pacer/ICD is shown, this is for illustration purposes only, and one of skill in the art could readily duplicate, eliminate or disable the appropriate circuitry in any desired combination to provide a device capable of treating the appropriate chamber(s) with cardioversion, defibrillation and pacing stimulation as well as providing for the aforementioned apnea detection and therapy. The housing **640** for pacer/ICD **10**, shown schematically in FIG. **17**, is often referred to as the "can", "case" or "case electrode" and may be programmably selected to act as the return electrode for all "unipolar" modes. The housing **640** may further be used as a return electrode alone or in combination with one or more of the coil electrodes, **628**, **636** and **638**, for shocking purposes. The housing **640** further includes a connector (not shown) having a plurality of terminals, **642**, **643**, **644**, **646**, **648**, **652**, **654**, **656** and **658** (shown schematically and, for convenience, the names of the electrodes to which they are connected are shown next to the terminals). As such, to achieve right atrial sensing and pacing, the connector includes at least a right atrial tip terminal (A_R TIP) **642** adapted for connection to the atrial tip electrode **622** and a right atrial ring (A_R RING) electrode **643** adapted for connection to right atrial ring electrode **643**. To achieve left chamber sensing, pacing and shocking, the connector includes at least a left ventricular tip terminal (V_L TIP) **644**, a left atrial ring terminal (A_L RING) **646**, and a left atrial shocking terminal (A_L COIL) **648**, which are adapted for connection to the left ventricular ring electrode **626**, the left atrial tip electrode **627**, and the left atrial coil electrode **628**, respectively. To support right chamber sensing, pacing and shocking, the connector further includes a right ventricular tip terminal (V_R TIP) **652**, a right ventricular ring terminal (V_R RING) **654**, a right ventricular shocking terminal (R_V COIL) **656**, and an SVC shocking terminal (SVC COIL) **658**, which are adapted for connection to the right ventricular tip electrode **632**, right ventricular ring electrode **634**, the RV coil electrode **636**, and the SVC coil electrode **638**, respectively. Separate terminals (not shown) may be provided for connecting the implanted warning/reminder device **18** and the implanted drug pump **20**, which are instead shown coupled directly to internal functional components of the pacer/ICD that control these devices. (The warning/reminder device is so named as it can be programmed to deliver reminders to the patient to take certain medications, as well as to deliver warnings as to medical conditions such as apnea.)

At the core of pacer/ICD **10** is a programmable microcontroller **660**, which controls the various modes of stimulation therapy. As is well known in the art, the microcontroller **660** (also referred to herein as a control unit) typically includes a microprocessor, or equivalent control circuitry, designed specifically for controlling the delivery of stimulation therapy and may further include RAM or ROM memory, logic and timing circuitry, state machine circuitry, and I/O circuitry. Typically, the microcontroller **660** includes the ability to process or monitor input signals (data) as controlled by a program code stored in a designated block of memory. The details of the design and operation of the microcontroller **660** are not critical to the invention. Rather, any suitable microcontroller **660** may be used that carries out the functions described herein. The use of microprocessor-based control circuits for performing timing and data analysis functions are well known in the art.

As shown in FIG. **17**, an atrial pulse generator **670** and a ventricular/impedance pulse generator **672** generate pacing stimulation pulses for delivery by the right atrial lead **620**, the right ventricular lead **630**, and/or the coronary sinus lead **624** via an electrode configuration switch **674**. It is understood that in order to provide stimulation therapy in each of the four chambers of the heart, the atrial and ventricular pulse generators, **670** and **672**, may include dedicated, independent pulse generators, multiplexed pulse generators or shared pulse generators. The pulse generators, **670** and **672**, are controlled by the microcontroller **660** via appropriate control signals, **676** and **678**, respectively, to trigger or inhibit the stimulation pulses.

The microcontroller **660** further includes timing control circuitry (not separately shown) used to control the timing of such stimulation pulses (e.g., pacing rate, atrio-ventricular (AV) delay, atrial interconduction (A-A) delay, or ventricular interconduction (V-V) delay, etc.) as well as to keep track of the timing of refractory periods, blanking intervals, noise detection windows, evoked response windows, alert intervals, marker channel timing, etc., which is well known in the art. Switch **674** includes a plurality of switches for connecting the desired electrodes to the appropriate I/O circuits, thereby providing complete electrode programmability. Accordingly, the switch **674**, in response to a control signal **680** from the microcontroller **660**, determines the polarity of the stimulation pulses (e.g., unipolar, bipolar, combipolar, etc.) by selectively closing the appropriate combination of switches (not shown) as is known in the art.

Atrial sensing circuits **682** and ventricular sensing circuits **684** may also be selectively coupled to the right atrial lead **620**, coronary sinus lead **624**, and the right ventricular lead **630**, through the switch **674** for detecting the presence of cardiac activity in each of the four chambers of the heart. Accordingly, the atrial (ATR. SENSE) and ventricular (VTR. SENSE) sensing circuits, **682** and **684**, may include dedicated sense amplifiers, multiplexed amplifiers or shared amplifiers. The switch **674** determines the "sensing polarity" of the cardiac signal by selectively closing the appropriate switches, as is also known in the art. In this way, the clinician may program the sensing polarity independent of the stimulation polarity. Each sensing circuit, **682** and **684**, preferably employs one or more low power, precision amplifiers with programmable gain and/or automatic gain control, bandpass filtering, and a threshold detection circuit, as known in the art, to selectively sense the cardiac signal of interest. The automatic gain control enables pacer/ICD **10** to deal effectively with the difficult problem of sensing the low amplitude signal characteristics of atrial or ventricular fibrillation. The outputs of the atrial and ventricular sensing circuits, **682** and **684**, are connected to the microcontroller **660** which, in turn, are able to trigger or inhibit the atrial and ventricular pulse generators, **670** and **672**, respectively, in a demand fashion in response to the absence or presence of cardiac activity in the appropriate chambers of the heart.

For arrhythmia detection, pacer/ICD **10** utilizes the atrial and ventricular sensing circuits, **682** and **684**, to sense cardiac signals to determine whether a rhythm is physiologic or pathologic. As used herein "sensing" is reserved for the noting of an electrical signal, and "detection" is the processing of these sensed signals and noting the presence of an arrhythmia. The timing intervals between sensed events (e.g., P-waves, R-waves, and depolarization signals associated with fibrillation which are sometimes referred to as "F-waves" or "Fib-waves") are then classified by the microcontroller **660** by comparing them to a predefined rate zone limit (i.e., bradycardia, normal, atrial tachycardia, atrial fibrillation, low rate VT, high rate VT, and fibrillation rate zones) and various other characteristics (e.g., sudden onset, stability, physiologic sen-

sors, and morphology, etc.) in order to determine the type of remedial therapy that is needed (e.g., bradycardia pacing, antitachycardia pacing, cardioversion shocks or defibrillation shocks).

Cardiac signals are also applied to the inputs of an analog-to-digital (A/D) data acquisition system **690**. The data acquisition system **690** is configured to acquire intracardiac electrogram signals, convert the raw analog data into a digital signal, and store the digital signals for later processing and/or telemetric transmission to an external device **702**. The data acquisition system **690** is coupled to the right atrial lead **620**, the coronary sinus lead **624**, and the right ventricular lead **630** through the switch **674** to sample cardiac signals across any pair of desired electrodes. The microcontroller **660** is further coupled to a memory **694** by a suitable data/address bus **696**, wherein the programmable operating parameters used by the microcontroller **660** are stored and modified, as required, in order to customize the operation of pacer/ICD **10** to suit the needs of a particular patient. Such operating parameters define, for example, pacing pulse amplitude or magnitude, pulse duration, electrode polarity, rate, sensitivity, automatic features, arrhythmia detection criteria, and the amplitude, waveshape and vector of each shocking pulse to be delivered to the patient's heart within each respective tier of therapy. Other pacing parameters include base rate, rest rate and circadian base rate.

Advantageously, the operating parameters of the implantable pacer/ICD **10** may be non-invasively programmed into the memory **694** through a telemetry circuit **700** in telemetric communication with the external device **702**, such as a programmer, transtelephonic transceiver or a diagnostic system analyzer. The telemetry circuit **700** is activated by the microcontroller by a control signal **706**. The telemetry circuit **700** advantageously allows intracardiac electrograms and status information relating to the operation of pacer/ICD **10** (as contained in the microcontroller **660** or memory **694**) to be sent to the external device **702** through an established communication link **704**. Pacer/ICD **10** further includes an accelerometer or other physiologic sensor **708**, commonly referred to as a "rate-responsive" sensor because it is typically used to adjust pacing stimulation rate according to the exercise state of the patient. However, the physiological sensor **708** may, depending upon its capabilities, further be used to detect changes in cardiac output, changes in the physiological condition of the heart, or diurnal changes in activity (e.g., detecting sleep and wake states) and to detect arousal from sleep. Accordingly, the microcontroller **660** responds by adjusting the various pacing parameters (such as rate, AV Delay, V-V Delay, etc.) at which the atrial and ventricular pulse generators, **670** and **672**, generate stimulation pulses. While shown as being included within pacer/ICD **10**, it is to be understood that the sensor **708** may also be external to pacer/ICD **10**, yet still be implanted within or carried by the patient. A common type of rate responsive sensor is an activity sensor incorporating an accelerometer or a piezoelectric crystal, which is mounted within the housing **640** of pacer/ICD **10**. Other types of physiologic sensors are also known, for example, sensors that sense the oxygen content of blood, respiration rate and/or minute ventilation, pH of blood, ventricular gradient, etc.

The pacer/ICD additionally includes a battery **710**, which provides operating power to all of the circuits shown in FIG. **17**. The battery **710** may vary depending on the capabilities of pacer/ICD **10**. If the system only provides low voltage therapy, a lithium iodine or lithium copper fluoride cell may be utilized. For pacer/ICD **10**, which employs shocking therapy, the battery **710** should be capable of operating at low current drains for long periods, and then be capable of providing high-current pulses (for capacitor charging) when the patient requires a shock pulse. The battery **710** should also have a predictable discharge characteristic so that elective replacement time can be detected. Accordingly, pacer/ICD **10** is preferably capable of high voltage therapy and batteries or other power sources appropriate for that purpose are employed.

As further shown in FIG. **17**, pacer/ICD **10** is shown as having an impedance measuring circuit **712** which is enabled by the microcontroller **660** via a control signal **714**. Other uses for an impedance measuring circuit include, but are not limited to, lead impedance surveillance during the acute and chronic phases for proper lead positioning or dislodgement; detecting operable electrodes and automatically switching to an operable pair if dislodgement occurs; measuring respiration or minute ventilation; measuring thoracic impedance for determining shock thresholds; detecting when the device has been implanted; measuring stroke volume; and detecting the opening of heart valves, etc. The impedance measuring circuit **120** is advantageously coupled to the switch **74** so that any desired electrode may be used.

In the case where pacer/ICD **10** is intended to operate as an implantable cardioverter/defibrillator (ICD) device, it detects the occurrence of an arrhythmia, and automatically applies an appropriate electrical shock therapy to the heart aimed at terminating the detected arrhythmia. To this end, the microcontroller **660** further controls a shocking circuit **716** by way of a control signal **718**. The shocking circuit **716** generates shocking pulses of low (up to 0.5 joules), moderate (0.5-10 joules) or high energy (11 to 40 joules), as controlled by the microcontroller **660**. Such shocking pulses are applied to the heart of the patient through at least two shocking electrodes, and as shown in this embodiment, selected from the left atrial coil electrode **628**, the RV coil electrode **636**, and/or the SVC coil electrode **638**. The housing **640** may act as an active electrode in combination with the RV electrode **636**, or as part of a split electrical vector using the SVC coil electrode **638** or the left atrial coil electrode **628** (i.e., using the RV electrode as a common electrode). Cardioversion shocks are generally considered to be of low to moderate energy level (so as to minimize pain felt by the patient), and/or synchronized with an R-wave and/or pertaining to the treatment of tachycardia. Defibrillation shocks are generally of moderate to high energy level (i.e., corresponding to thresholds in the range of 5-40 joules), delivered asynchronously (since R-waves may be too disorganized), and pertaining exclusively to the treatment of fibrillation. Accordingly, the microcontroller **660** is capable of controlling the synchronous or asynchronous delivery of the shocking pulses.

Microcontroller **60** also includes an IEGM individual feature morphology-based respiration detector **701** for detecting respiration based upon one or more IEGM channel signals using the techniques described above. An abnormal respiration pattern detector **703** is also provided the purposes of detecting apnea, hypopnea, etc. using techniques described above. Additionally, an abnormal respiration therapy controller **705** is provided for controlling therapy in response to an episode of abnormal respiration, again using techniques already described. Depending upon the implementation, the various components may be implemented as separate software modules. However, the modules may be combined so as to permit single modules to perform multiple functions.

Further Abnormal Respiration Detection Techniques

Turning now to FIGS. **18-27**, techniques particularly directed to detecting abnormal respiration will be described.

The techniques may be used, for example, by the pacer/ICD of FIGS. **16-17** to implement step **450** of the technique of FIG. **14**.

An overview of these abnormal respiration detection techniques is set forth in FIG. **18**. Initially, at step **800**, the pacer/ICD identifies individual respiratory cycles within patient respiration, i.e. the pacer/ICD identifies individual breaths. Specific techniques for identifying individual respiratory cycles are discussed below with respect to FIGS. **19-22**. At step **802**, the pacer/ICD detects parameters associated with the individual respiratory cycles such as the inter-breath interval, respiration depth, standard deviation of respiration depth, median respiration depth, and respiration power. Specific techniques for detecting such parameters are discussed below with respect to FIGS. **23-24**. Next, at step **804**, the pacer/ICD detects any significant changes in the parameters associated with the individual respiratory cycles, i.e. the pacer/ICD detects any significant increase or decrease in the parameters. Depending upon the particular respiratory parameters and depending up on the particular form of abnormal respiration, the changes in the respiratory parameters may be abrupt or gradual. Specific techniques for detecting significant changes in respiratory parameters are discussed below with respect to FIG. **25**. Finally, at step **806**, the pacer/ICD, evaluates the significant changes to detect abnormal respiration. In this regard, normal respiration during sleep is characterized by little or no change in respiratory parameters such as respiration depth (when corrected for patient posture and other non-respiratory factors). Hence, significant changes in respiratory parameters such as respiration depth are indicative of, or associated with, a transition from normal respiration to some form of abnormal respiration. Specific threshold-based techniques for evaluating the changes to detect abnormal respiration are discussed below with respect to FIG. **25**. Once abnormal respiration is detected, various techniques may be used to identify the particular form of abnormal respiration, i.e. to distinguish among apnea, hypopnea, hyperpnea, CSR, etc. Exemplary techniques for distinguishing among different forms of abnormal respiration are discussed above in connection with FIG. **14**.

Turning now to FIGS. **19-20**, exemplary techniques for identifying individual respiratory cycles will be described for use at step **800** of FIG. **18**. At step **808**, the pacer/ICD inputs temporal and morphological parameters derived from the IEGM. This may include, e.g., the maximum amplitude, peak-to-peak amplitude, width and integral of individual features of the IEGM such as the intrinsic atrial depolarization events (P-waves), atrial evoked responses (AER), intrinsic ventricular depolarization events (QRS-complexes), ventricular evoked responses (VER) and premature ventricular events (PVEs). Other exemplary parameters include: the integral of the ventricular post depolarization signal (vPDI), the integral of the atrial post depolarization signal (aPDI), the repolarization integral (tI), a PDI derived from the ventricular far-field post depolarization signal (ffPDI), an integral of the repolarization far-field signal (fftI). Depending upon the signal, it may be appropriate to separately track near-field and far-field signals (particularly with regard to repolarization amplitudes.) Insofar as temporal parameters are concerned, any of a variety of inter-feature or intra-feature intervals may be tracked, such as, e.g., A-A intervals, AV intervals, R-R intervals, ST intervals, etc. Note that the evaluation of R-R interval is particularly helpful in detecting respiratory sinus arrhythmia (RSA), which is heart rate variability in synchrony with respiration.

It is important to correctly extract morphological and temporal variable from IEGM data to ensure that the variable properly reflects the respiratory modulation. A history of the morphological characteristics can be used to aid in variable extraction. FIG. **20** illustrates an exemplary cardiac cycle **809** including an R-wave (i.e. QRS complex) and a T-wave. Brackets illustrate a historical range of values for T-wave parameters such as T-wave amplitude and ST-interval. Historical ranges such as those illustrated in FIG. **20** may be used by the pacer/ICD to properly identify the parameter to be extract from the IEGM. For example, use of the T-wave amplitude range can be used by the pacer/ICD to correctly extract T-wave amplitude values.

At step **810**, the pacer/ICD examines the temporal and morphological parameters to detect any fused beats and to reject the parameters derived from fused beats, as these parameters may be anomalous. In one example, various sets of histogram bins are stored in memory and used to track the distribution of parameter values. Each memory bin is associated with a range of values. An exemplary set of bins for use with vPDI is illustrated in FIG. **21**. Whenever, a new vPDI value is detected, the pacer/ICD increments the bin corresponding to the new value. The histogram bins thereby quantify the distribution of vPDI values over a period of time. In the specific example of FIG. **21**, exemplary vPDI bin values **812** obtained over a six hour period of time are illustrated. (The vertical axis represents bin count. The horizontal axis represents PDI values along an arbitrary scale.) As can be seen, the majority of individual cardiac cycles have vPDI values in the range of 600 and 1200. Any vPDI value that deviates significantly from that range is likely the result of a fused beat and is preferably discarded. Depending upon the implementation, a set of histogram bins such as illustrated in FIG. **21** may be maintained for each temporal and morphological parameter. In other implementations, histogram bins are maintained only for selected cardiac cycle parameters. Otherwise routine experimentation may be employed to identify particular parameters that are advantageously tracked via histogram bins. Preferably, the parameters that are tracked via histogram bins are parameters that are strongly affected by fusion so as to permit fused beat to be readily detected and rejected. Parameters such as vPDI, aPDI, tI, ffPDI, and fftI are typically good candidates. Other techniques for detecting and rejecting fused beats may additionally or alternatively be employed.

At steps **814** and **816** of FIG. **19**, the pacer/ICD determines baseline values for the temporal and morphological parameters and corrects for any baseline shifts due to changes in posture. In one example, separate running averages for each of the parameters are tracked. The running average is used as current baseline. Parameters are corrected by subtracting the baseline from the values. Any significant drift in the running average is indicative of a change in posture or other change not due to respiratory variations. Other techniques may be used for detecting changes in posture such as techniques set forth in U.S. patent application Ser. No. 10/329,233, of Koh et al., entitled "System and Method for Determining Patient Posture Based On 3-D Trajectory Using an Implantable Medical Device", filed Dec. 23, 2002. Once a change in posture is detected, a new baseline value is calculated based on a running average of values of the parameter obtained after the change in posture. Preferably, all parameters used in detecting individual respiratory cycles for the purposes of detecting abnormal respiration are corrected for baseline shifts using there or other suitable correction techniques.

At step **818**, the pacer/ICD analyzes the corrected temporal and morphological parameters to identify individual respiratory cycles (i.e. breaths) based on cyclical changes therein. As already explained in connection with FIGS. **2-13**, the tempo-

ral and morphological parameters derived from the IEGM exhibit cyclical variations indicative of respiration. Hence, individual respiratory cycles (i.e. individual breaths) can be detected based on the correct temporal and morphological parameters. Otherwise conventional signal processing techniques may be used to identify cyclical changes in the corrected parameters that are representative of respiration.

FIG. **22** illustrates cyclical variations in tPDI (i.e. the paced depolarization integral associated with a T-wave) detected by a pacer/ICD along with externally derived signals representing patient respiration including: nasal flow **822**, chest expansion **824**, and abdominal expansion **826**. As can be seen, the tPDI signal exhibits cyclical variations that are correlated with patient respiration. These cyclical variations are detected to identify the individual respiratory cycles at step **818** of FIG. **19**. Note that the particular respiratory pattern shown in FIG. **22** exhibits CSR. The tPDI signal not only permits the individual respiratory cycles to be detected but also permits CSR to be detected, as will be described below with reference to FIGS. **25** and **26**. Note also that FIG. **22** additionally illustrates a power value **828** associated with the tPDI signal, which is helpful in detecting abnormal respiration and will also be described below.

Exemplary techniques for detecting respiratory parameters will now be described with respect to FIGS. **23-24**. These techniques may be used at step **802** of FIG. **18**. At step **830**, the pacer/ICD examines the individual respiratory cycles detected via the procedure of FIG. **19** to detect inter-breath intervals, i.e. the interval between peaks of consecutive respiratory cycles. At step **832**, the pacer/ICD then integrates the respiration pattern over each individual inter-breath interval to determine depth of respiration for each individual respiratory cycle. The respiratory pattern that is integrated is the signal from which the respiratory cycles were derived and hence can depend on the particular temporal or morphological parameters detected by the device. In the example of FIG. **22**, where tPDI is used to detect respiratory cycles, the tPDI signal is integrated over each respiratory cycle found therein. FIG. **24** illustrates an example where a vPDI signal **834** is instead detected during a period of CSR. In that example, the vPDI signal is integrated over each inter-breath interval found therein to obtain a respiration depth signal **835**. A single respiration depth value is obtained for each respiratory cycle. Otherwise conventional numerical integration techniques can be employed by the pacer/ICD. For comparison purposes, FIG. **24** also illustrates externally-derived respiratory signals: a chest signal **836**, an abdominal signal **838** and a nasal flow signal **840**, each tracking the periodic CSR pattern. As can be seen, the respiration depth signal **835** derived by integrating the vPDI signal **834** also exhibits with the CSR cyclical variations found in the externally-derived signals. Accordingly, respiration depth, by itself, can typically be used to detect abnormal respiration. However, to enhance reliability and specificity, the pacer/ICD preferably determines various other respiratory parameters.

At step **842** of FIG. **23**, the pacer/ICD evaluates the depth of respiration over multiple respiratory cycles to determine its standard deviation and median. Otherwise conventional statistical techniques may be employed to evaluate the standard deviation and the median. Other statistical values may additionally or alternatively be evaluated. At step **844**, the pacer/ICD determines "respiratory power" by summing respiration depth (**835** of FIG. **24**) over discrete temporal epochs. The epochs are preferably ten seconds each, but other durations may be used for the epochs such as values in the range of five to fifteen seconds. Hence, in one example, once every ten seconds the pacer/ICD sums the respiration depth values obtained during the previous ten second epoch. An exemplary, resulting respiratory power signal **846** is also shown in FIG. **24**. It too exhibits cyclical variations indicative of CSR. Note, however, because the respiratory power is derived based on the preceding ten seconds of respiratory depth signals, its cyclical variations tend to lag those exhibited in the respiration depth signal. At step **848**, the pacer/ICD stores the various values it has calculated: depth of respiration, standard deviation of the depth of respiration, median of depth of respiration, and power of respiration for use in detecting abnormal respiration and for subsequent diagnostic review. In addition to calculating a power value from the respiration depth, the pacer/ICD can also calculate a power value associated with each of the temporal and morphological parameters (such as aPDI, vPDI, etc.) by integrating these parameters over the last ten second epoch. (This is discussed further with reference to FIG. **27**.) The additional power values may be combined with the respiration power to provide a more robust power value for use in abnormal respiration detection.

Turning now to FIG. **25**, exemplary techniques for detecting significant changes in the respiratory parameters will be described for use at step **804** of FIG. **18**. At step **850**, the pacer/ICD detects gradual and/or abrupt changes in the respiratory parameters, i.e. in one or more of depth of respiration, standard deviation of the depth of respiration, median of depth of respiration, and power of respiration. Otherwise conventional signal processing techniques can be used to detect changes, such as evaluating a time derivative of the signal, which represents a rate of change of the signal with time. The faster the rate of change, the more abrupt the change in the parameter. Depending upon the implementation, it may be desirable to combine two or more respiratory parameters into a signal for evaluation. As noted, however, the respiratory power signal lags the other signals and hence care should be taken if combining the power signal with the other signals. In any case, at step **852**, the pacer/ICD quantifies the magnitude of the change. In one example, the magnitude of the change is simply the post-change value of the respiratory parameters (or combination of parameters) minus the pre-change value.

FIG. **26** illustrates a technique for evaluating the changes to the respiratory parameters to detect abnormal respiration for use at step **806** of FIG. **18**. Ate step **854**, the pacer/ICD compares the magnitude of the changes against one or more thresholds indicative of abnormal respiration. For example, if the respiratory parameter being tracked is the depth of respiration, the magnitude of any abrupt change in respiration depth is compared against a predetermined threshold indicative of abnormal respiration. The thresholds depend on the particular parameter being tracked and may further vary from patient to patient. Suitable threshold values may be specified following implant of device based on the specific characteristics of patient in which the device is implanted and/or may be automatically updated during routine working of the algorithm. The direction of the change is also preferably analyzed to determine whether an episode of abnormal respiration is beginning or ending. For example, a sudden drop in respiration depth from a previously normal depth is indicative of the onset of apnea/hypopnea. A sudden increase in respiration depth from a previously abnormally low respiration depth is instead indicative of a return to normal respiration. A still further abrupt increase may be indicative of the onset of hyperpnea. At step **856**, the pacer/ICD then generates signals indicative of onset or termination of abnormal respiration. The signals may be used to trigger warning signals or to control therapy, as already described above with reference to FIG. **14**. Also, as has already been explained in connection with FIG. **14**, the pacer/ICD preferably identifies the particu-

lar form of abnormal respiration so as to permit the appropriate therapy and/or warnings to be delivered.

FIG. **27** further illustrates and summarizes the components and method steps employed to implement the technique of FIGS. **18-26**. As will be explained, the technique of FIG. **27** includes some additional features as well. Briefly, raw IEGM data **900** is filtered via sense amplifiers **902** to yield sense amplifier data **904**. The sense amplifier data is analyzed via an event identification block **906** to identify and extract individual events **908**, such as paced atrial or ventricular events and intrinsic (i.e. sensed) atrial and ventricular events. These steps/components are conventional. Then, the raw IEGM data and the events found therein are processed at block **910** to extract variables for the purposes of abnormal respiration detection. That is, data and signal from all available IEGM channels of cardiac rhythm management (CRM) device, i.e. the pacer/CD, are extracted. Examples include: R-R, P-P, PDI, QT interval, aPDI, vPDI, ffPDI, tI, fftI etc. At block **912**, the pacer/CD derives or calculates distributions for the various variables. The histogram techniques described above with reference to FIG. **21** may be employed to derive the distributions. At block **914**, the pacer/CD calculates and removes respective baseline means, preferably using techniques described above with reference to steps **814** an **816** of FIG. **19**. At block **915**, the pacer/ICD preferably normalizes the variables to remove body position-based variability. In one example, a running average of the mean and the standard-deviation are maintained with a window of width equal to 64 beats, i.e. i−64 to i+64. An i+64 scheme is preferable to using an i−128 to i scheme to prevent lag due to such calculation. The IEGM variables are then normalized by eliminating any variation in the calculated mean and standard-deviation. In one specific example, the following formula is used:

$$x_i' = \frac{x_i - \mu}{\sigma} i \in N$$

where □=local mean, and where the local standard deviations are used. In this manner, a moving window normalization is achieved to remove the mean and standard-deviation changes that occur due to body position changes while retaining the relative variations due to respiration.

At block **916**, the pacer/CD calculates the power of each variable over a previous epoch of X seconds (e.g. 10 seconds.) This is performed by integrating the variable over the previous epoch of time. These power values are in addition to the respiration power value that is described above with reference to FIG. **23** and provide a further set of values to aid in detecting abnormal respiration. At block **918**, the pacer/ICD evaluates the breathing interval, i.e. the inter-breath interval or interval between peaks of consecutive respiratory cycles. Once the breathing interval is calculated, the pacer/ICD can then evaluate respiratory power, which is a sum of respiration depth over the preceding epoch of time where a single respiration depth value is calculated for each individual breathing interval.

At block **922**, the pacer/ICD compares the various derived parameters and one or more thresholds, as described above with reference to FIGS. **25** and **26** to detect abnormal respiration. At block **924**, individual events (i.e. individual episodes of abnormal respiration) are detected and appropriate diagnostics are stored. Also, as already explained, appropriate therapy may be applied and/or warning signals may be generated.

The techniques of FIGS. **18-27** are advantageously performed while the patient is asleep to detect nocturnal forms of abnormal respiration, but may potentially be performed while awake. (CSR, for example, can occur while a patient is awake, particularly if CHF is severe.) In implementations wherein the techniques are implemented only while the patient is asleep, otherwise conventional sleep detection techniques may be used to detect the onset and termination of sleep. In addition, the sleep detection techniques of the Bornzin et al. and Park et al., patents, cited above, may be used. Additionally, or in the alternative, respiratory parameters detected by the techniques described herein—such as depth of respiration—may be used to detect sleep. In this regard, sleep, compared with wakefulness is associated with reduced lung ventilation mainly due to decreases in tidal volume. Accordingly, detection of persistent low respiration depth can be used alone, or in combination with other techniques, to detect sleep. (A respiration profile incorporating a period of sleep is illustrated in FIG. **15** and described above.)

Also, whereas the techniques of FIGS. **18-27** are advantageously employed in "real time" (based on IEGM signals as they are sensed), the technique can alternatively be employed based on previously recorded parameters. For example, data may be collected overnight then analyzed later to detect episodes of abnormal respiration that have already occurred for the purpose of generate appropriate diagnostic data for physician review.

Pattern Classifier-Based Abnormal Respiration Detection Techniques

Turning now to FIGS. **28-35**, additional techniques will be described for discriminating normal and abnormal respiration (particularly apnea/hypopnea). Among other innovations, these techniques utilize pattern classifiers trained to detect abnormal respiration based on features of IEGM signals.

FIG. **28** provides an overview of IEGM-based abnormal respiration detection techniques employing pattern classifiers. Beginning at step **1000**, the pacer/ICD senses IEGM signals (or other appropriate electrical cardiac signals) and identifies individual cardiac cycles therein. (This step is, of course, routinely performed by the pacer/ICD whether or not IEGM-based respiration detection is performed.) At step **1004**, the pacer/ICD detects one or more parameters from the cardiac cycles. The parameters can include morphological metrics such as various PDI values, as well as interval-based metrics such as P-R and R-R intervals. As will be explained below, the parameters can be further processed to extract time-domain features (such as mean or standard deviation values) and frequency domain features (such as a power spectral density value). In any case, the parameters (or features derived therefrom) are applied to a device trained to discriminate between normal and abnormal respiration such as a pattern classifier, at step **1006**, so as to detect abnormal respiration, if any, within the patient. In some implementations, the method of FIG. **28** is performed to determine whether the patient is subject to abnormal respiration but does not specifically identify individual episodes of abnormal respiration. Rather, diagnostic data is recorded for physician review, which indicates that the patient is subject to abnormal respiration. In other implementations, the method is performed to identify individual episodes of abnormal respiration such as individual episodes of apnea/hypopnea. In any case, a wide variety of devices and/or algorithms may be trained to discriminate between normal and abnormal respiration. In the following examples, one or more pattern classifiers are used.

The pattern classifier can alternatively be trained to discriminate among normal respiration, CSA and OSA. A clas-

sifier trained to discriminate between normal and abnormal respiration is referred to herein as 2-class pattern classifier. A classifier trained to discriminate among normal respiration, CSA and OSA is referred to herein as 3-class pattern classifier. In other examples, the pattern classifier may be configured to discriminate among still further types of abnormal respiration, such as CSR. That is, a 4-class, 5-class (or N-class) pattern classifier may instead be used. In any case, by using a pattern classifier or similar device, respiratory discrimination can be readily and reliably achieved. Linear discriminant pattern classifiers for detecting apnea based on EKG signals are described in the aforementioned patent to de Chazal, et al., cited above. Technique described therein may be adapted to discriminate different types of respiration based instead on IEGM signals or other internally sensed electrical cardiac signals as in FIG. **28**. Techniques employing pattern classifiers are also discussed in the co-pending application filed contemporaneously herewith, also cited above. See, also, U.S. Patent Application 2006/0184056 of de Chazal et al., entitled "Apparatus for Detecting Sleep Apnea using Electrocardiogram Signals."

Note that, although the pattern classifier techniques described herein are particularly well-suited to detecting abnormal respiration such as CSA or OSA, other normal or abnormal physiologic states may be detected as well. Other physiologic states that potentially may be detected, tracked and discriminated using a pattern classifier include hyperpnea, asthma, CSR, hypoglycemia, hyperglycemia, diabetes, renal failure, hypertension, ischemia, hyperkalemia, hypokalemia, obesity, stroke, chronic obstructive pulmonary disease (COPD), pulmonary edema, edema, anemia, heart failure, exertion induced dyspnea, and tachypnea with hypoglycemia. That is, the implantable device is equipped to detect a variety of cardiac disease comorbidities. In this regard, if a patient is a predisposed toward one cardiac disease, the patient is also predisposed to other diseases or conditions, referred to as comorbidities. Pacer/ICDs are usually implanted in response to some form of cardiac ailment or disease. Accordingly, patients with pacer/ICDs are often predisposed to the aforementioned comorbidities and hence it is desirable to detect the physiologic states associated therewith. Detection of these other cardiac disease comorbidities are discussed in greater detail in the co-pending application filed contemporaneously herewith, also cited above.

Turning now to FIGS. **29-30**, an illustrative technique employing a 3-class pattern classifier for detecting abnormal respiration will now be described. Steps for training the pattern classifier are shown in FIG. **29**. Steps for using the pattern classifier (once trained) are shown in FIG. **30**. Training is preferably performed prior to device implant. That is, a single pattern classifier is trained in advance using IEGM data collected from a population of test subjects, then individual trained classifiers are installed in various pacer/ICDs for use with individual patients. Alternatively, the pattern classifier of a particular pacer/ICD is trained for the particular patient in whom it is implanted based on IEGM data sensed within that particular patient. The examples of FIGS. **29-30** are directed to implementations where a single classifier is trained in advance based on IEGM data collected from a population of test subjects. Two general implementations for training and using the pattern classifier are covered herein. In a first implementation, the pattern classifier is trained to determine whether or not a patient suffers from abnormal respiration. In a second implementation, the pattern classifier is instead trained to identify individual episodes of abnormal respiration. In the first implementation, the pattern classifier is trained by applying IEGM signals from test subjects to the pattern classifier along with an indication of whether particular test subjects suffer from abnormal respiration or not. The pattern classifier is thereby trained to discriminate between patients suffering from abnormal respiration (i.e. the patients have a significant number of episodes of abnormal respiration) and patients with normal respiration (i.e. the patients do not have any significant number of episodes of abnormal respiration). In the second implementation, the pattern classifier is trained by applying IEGM signals from test subjects to the pattern classifier along with an indication of whether particular test subject is currently suffering from an episode of abnormal respiration. The pattern classifier is thereby trained to discriminate normal respiration from episodes of abnormal respiration so as to allow individual episodes of abnormal respiration to be detected. In the following examples, it is assumed that the first implementation is employed, unless indicated otherwise.

Beginning at step **1100** of FIG. **29**, the training system first determines whether the patient is asleep (or is otherwise inactive) and hence potentially subject to sleep apnea or other abnormal respiration disorders occurring during sleep, referred to generally as sleep disordered breathing (SDB). Otherwise conventional sleep detection techniques may be used. (In this example, the pattern classifier is only employed within patients while they are asleep and so training is only performed based on cardiac cycles detected while the test subjects are also asleep. In other examples, it may not be necessary to wait until the patients and test subjects are asleep.) Assuming the test subject is asleep, the training system, at step **1102**, receives atrial and ventricular IEGM signals initially sensed within the test subject (by, for example, a conventional pacemaker already implanted therein) and identifies individual events within the IEGM signals including: P-waves, R-waves (i.e. QRS-complexes), T-waves, AERs, and VERs. Conventional detection techniques may be used to detect the events, and conventional event markers may be used to designate and record the events.

At step **1104**, the training system extracts or otherwise detects various morphological parameters or "metrics" from the identified events. Morphological parameter examples include: vPDI, tPDI, aPDI, ffPDI, and fftPDI. The parameters vPDI and aPDI are described above with reference to FIG. **19**. The parameter tPDI represents a T-wave-based integral (and is also referred to above as a tI value.) The parameter fftPDI represents a far-field tPDI (and is also referred to above as an fftI value.) Other examples of morphological parameters include: the maximum amplitude, peak-to-peak amplitude and width of the events of the cardiac signals. The particular morphological parameters to be extracted from the cardiac signals depend upon the current programming of the training system. At step **1106**, the training system then extracts or otherwise detects various interval-based parameters or metrics from the identified events. Interval-based parameter examples include: R-R, P-R, P-P and QT intervals. As with the morphological parameters, the particular intervals to be extracted from the cardiac signals for use in training the pattern classifier depends upon the current programming of the training system.

At step **1108**, the training system inputs the respiratory status of the test subject (i.e. whether the test subject generally suffers from OSA or CSA or instead had normal respiration). This is appropriate if the pattern classifier is to be trained to determine whether a patient is subject to OSA or CSA without necessarily detecting individual episodes. The diagnosis of OSA or CSA can be achieved using an otherwise conventional external respiration detection system. (Alternatively, the training system inputs an indication of whether the test

subject is currently suffering from an episode of OSA or CSA so it can be trained to specifically detect individual episodes.) At step **1110**, the training system then trains a 3-class pattern classifier to discriminate between normal respiration, CSA and OSA by applying (1) the extracted parameters and (2) the indication of the current respiratory state of the patient to the pattern classifier. Otherwise conventional techniques may be employed to configure the pattern classifier so that it can learn to discriminate among normal respiration, CSA and OSA based on the input parameters (or based on time-domain and frequency domain features extracted from the parameters as discussed below.)

Once a sufficient amount of data has been processed for a particular test subject, a new test subject is selected, at step **1111**, and the training procedure is repeated for the new test subject. Typically, a fairly large number of cardiac cycles from a large number of test subjects—some having normal respiration, others subject to CSA, and still others subject to OSA—should be applied to the pattern classifier during the technique of FIG. **29** to train the classifier. Eventually, once training is complete (and the classifier has been properly tested to verify its reliability) the classifier is downloaded within pacer/ICDs for implant within patients so that the he pattern classifier may then be employed to determine whether individual patients have abnormal respiration. That is, the trained classifier parameters are hard-coded into a device for implant. In some implementations, however, the trained classifier parameters are merely used as initial parameters within each individual patient. The particular classifier within a given patient can then be further trained based on IEGM signals detected within that patient so as to optimize the classifier for that patient. Also, other clinical inputs can be applied to the pattern classifier within a particular patient so as to optimize the parameters of the classifier for that particular patient. Examples include 1) Epworth Sleepiness Score (or similar test of sleepiness; 2) an indication of whether the patient snores; 3) an indication of whether the patient is known to exhibit pauses during sleep; 4) an indication of whether the patient has LV dysfunction; 5) the ejection fraction (EF) of the patient; 6) an indication of whether the patient has hypertension; 7) systolic/diastolic pressure; 8) an indication of whether the patient has AF; 9) an indication of whether the patient has heart failure. The pattern classifier can also be used in combination with various sensors to augment its performance. Exemplary sensed metrics include dynamic impedance (Z) values and SpO_2 and SvO_2 values. See, for example, U.S. patent application Ser. No. 10/795,009, of Koh, entitled "System and Method for Distinguishing among Obstructive Sleep Apnea, Central Sleep Apnea and Normal Sleep Using an Implantable Medical System," filed Mar. 4, 2004. These additional metrics can also be used during initial training by outputting the sensor signals from a pacer/ICD within a test subject to the training system. The training system then trains the pattern classifier, in part, using the additional sensor metrics.

FIG. **30** illustrates the use of a pattern classifier trained by the techniques of FIG. **29**. Beginning at step **1112**, a pacer/ICD that has a trained pattern classifier installed therein determines whether the patient (in which it has been installed) is asleep or otherwise inactive so as to trigger activation of the pattern classifier. Preferably, the pattern classifier is not activated under conditions, such as during AF/AT, that were excluded when the classifier was trained. This is also discussed in the co-pending application. Assuming the pattern classifier is activated, step **1114** is then performed wherein the pacer/ICD senses IEGM signals and identifies individual events therein: P-waves, R-waves, etc. At steps **1116** and **1118**, the pacer/ICD extracts the same types of morphological and interval-based parameters initially used to train the pattern classifier. As explained, in at least some patients, only one or two parameters may need be extracted. At step **1120**, the pacer/ICD then detects and discriminates OSA and CSA by applying the extracted parameters to the trained pattern classifier. In this regard, the pattern classifier may be configured to generate indices representative of the degree of OSA and CSA. If the OSA index exceeds an OSA threshold, the patient is subject to OSA. Conversely, if the CSA index exceeds a CSA threshold, the patient is subject to CSA. At step **1122**, the pacer/ICD also preferably determines the severity of OSA or CSA within the patient. The aforementioned indices may also be used to evaluate severity. That is, the higher the index, the more severe the condition. The severity of CSA or OSA may also be ascertained using otherwise conventional techniques, such as by determining the duration of each period of apnea. At step **1124**, the pacer/ICD records diagnostic information and, depending upon the capabilities of the pacer/ICD, also delivers appropriate therapy and/or generates warning signals.

Note that, depending upon the particular patient, some parameters may be more effective in the discrimination process. Parameters that are not effective may potentially be ignored by the pacer/ICD for the purposes of abnormal respiration detection within that particular patient, thereby reducing processing requirements. In at least some cases, only one or two parameters—such as only one morphology metric and only one interval metric—are needed. For some patients, only morphological parameters might be required whereas, in other patients, only interval-based parameters might be required. Also, note that parameters detected during certain conditions, such as atrial fibrillation (AF) or atrial tachycardia (AT), may be excluded during the training procedure. Insofar as AF is concerned, if AF is not found to add a significant confounding component to the ventricular channel IEGM morphology, then the training system need not exclude the AF data. E.g., if the ventricular pacing and rate is maintained during episodes of AF, and if the respiration component is still visible from the ventricular IEGM morphology metrics, the training system preferably does not exclude data collected during AF. This is discussed in greater detail in the co-pending application filed contemporaneously herewith, cited above.

FIG. **31** illustrates how apnea training and detection techniques of FIGS. **29-30** might be activated while a patient is asleep (or otherwise inactive.) That is a "region of interest" **1126** coincides with a sleep period of the patient, as determined by a running average of breathing rates **1128** and a running average of activity levels **1130**. Note that the patient is not necessarily asleep continuously during this period of time. Indeed, if suffering frequent episodes of frank apnea, the patient will likely wake up frequent as a result of those episodes. Moreover, as already explained, the pattern classifier need not be limited for use while the patient is asleep and hence the use of a sleep detector and/or activity sensor is optional. Various other techniques may be employed to perform "sleep gating", particularly techniques using additional parameters to detect sleep.

Turning now to FIG. **32**, a more detailed example of the usage of a pattern classifier is illustrated. This example employs a 2-class pattern classifier that has already been trained to discriminate between apnea and normal respiration. The trained pattern classifier is installed within a pacer/ICD implanted within a patient. Initially, separate atrial and ventricular channel IEGM signals **1200** and **1202** are acquired within the patient in a unipolar, bipolar, or multipo-

lar lead configuration. The IEGM signals are input by the pacer/ICD (schematically denoted within FIG. **32** by cardiac rhythm management (CRM) device block **1204**.) The pacer/ICD analyzes the IEGM data to generate atrial and ventricular event markers and to identify particular windows or portions of the IEGM. In particular, the pacer/ICD identifies one-minute long epochs, which will be used in processing the data. R-R, P-R, P-P and QT intervals are detected, at block **1206**. (The R-R, P-R, P-P intervals may be easily determined from the P and R event makers. The QT interval may require further processing of the IEGM to identify the Q-point of the QRS-complex (i.e. R-wave) and to further identify the T-wave.) At block **1208**, PDI metrics are derived from the IEGM. As noted, not all of these PDIs need be calculated. Rather, the PDI of the cardiac cycle component that best represents the respiration cycle in the patient may instead be chosen. The integral calculation may be identical to the calculation of the PDI for evoked response evaluation in current CRM devices. Specific techniques for deriving metrics from IEGM signals that best represent respiration are discussed above in connection with FIGS. **1-27**.

At block **1210**, a one-minute epoch of morphological and interval metrics is stored in a buffer. Before storage, the data may first be normalized to achieve zero mean and unit standard-deviation. At block **1212**, individual time domain features are extracted, such as mean and standard deviations. Individual frequency domain features are also extracted, such as power spectral density metrics. In this example, the feature data extracted at block **1212** is the data that is actually applied to the pattern classifier (and hence is also the data used to initially train the pattern classifier.) In this regard, a pattern classifier model has already been trained on a pre-existing database of IEGM signals to provide a probability of each test epoch period containing episodes of apnea/hypopnea or not. As already noted, the classifier can be trained in multiple ways, and can be invoked based on the focus of the algorithm. In a 2-class problem classification, the model is trained to identify normal events from apnea/hypopnea events. In a 3-class problem, the model is trained to identify normal events v/s obstructive events and central events individually. This is helpful in identifying the type of predominant underlying apnea, so that the screening along with the apnea severity and apnea type can provide more information to the physician as to an appropriate mode of treatment for the patient.

Additionally, note that the features incorporated for different cardiac rhythm types may be the same, or can be set differently. For example, it may be determined that patients with rhythm type PR should have features derived from vPDI, and the patients with rhythm type AV should have the features derived from tPDI. (Cardiac rhythm types are discussed in greater detail below with reference to FIGS. **33-34**. Cardiac rhythm types are also discussed in the co-pending application filed contemporaneously herewith.) Also, classifier parameters for different rhythm types may be the same, or can be set differently. For example, the classifier can be trained on different rhythm type separately such as: different training for AR, PR, AV, PV rhythm types, or AR+AV and PR+PV combined together, and the corresponding classifier parameters can be stored and invoked when the specific rhythm type is encountered. At block **1214**, discriminant values are calculated for each class of the 2-class patter classifier based on the features derived from the latest one-minute epoch of data. In one example, the discriminants y_k are of the form: y_k=a*x+b+log(prior-probability), wherein a and b are constants from the classifier model (i.e. from the trained pattern classifier), and log(prior-probability) is a fixed value that can all be stored in the CRMD device as constants. For example,

$$a=-0.5*\text{transpose}(\square_k)*inv(CV)$$

$$b=-0.5*\text{transpose}(\square_k)*inv(CV)*\square_k$$

wherein CV represents a covariance matrix and $\square_k$ represents suitable constants. CV is constant in a similar manner that $\square_k$ is a constant. The class that produces the highest value of y_k is then chosen as the correct class for the epoch (and which thereby discriminates normal respiration from abnormal respiration.) As already noted, various clinical inputs may be used to optimize a pattern classifier for a particular patient. That is, it is possible to "bias" a patient e.g. modify the prior-probability, based on clinical condition determination e.g. Epworth sleepiness scale input, hypertension, CHF etc. The same or similar equations listed above can be used in a 3-way classifier.

At block **1216**, the posterior probabilities are combined so as to form a diagnostic measure, i.e. an index representing the measure of severity of apnea/hypopnea. In one example, the sum of the number of epochs with the class type "apnea/hypopnea" is then used to form the diagnostic measure of the index representing the measure of severity of apnea/hypopnea within the patient. If the index is clinically significant (i.e. the index exceeds a predetermined threshold indicative of "clinical significance"), the patient is thereby screened as being apneic/hypopneic (i.e. the patient is subject to apnea/hypopnea), at block **1218**. Otherwise, the patient is screened as being non-apneic/hypopneic (i.e. the patient is not subject apnea/hypopnea), at block **1220**. As already explained, apnea can be further discriminated between OSA and CSA by instead employing a 3-class pattern classifier.

Hence, in this example, the pattern classifier is not used to identify individual episodes of apnea/hypopnea but to instead determine whether the patient is generally prone or subject to such episodes. Hence, the pattern classifier provides a preliminary diagnosis of whether the patient suffers from apnea/hypopnea. Appropriate diagnostics information is stored for physician review. The physician makes the final determination of whether the patient indeed suffers from apnea/hypopnea and initiates appropriate therapy. In other implementations, the pattern classifier is trained and used to detect individual episodes of apnea/hypopnea.

Turning now to FIGS. **33-34**, an illustrative technique will be described wherein the current cardiac rhythm type of the patient is taken into account. Steps for training one or more pattern classifiers using a training system are shown in FIG. **33**. Steps for using a trained pattern classifier(s) installed within a pacer/ICD are set forth in FIG. **34**. Many of the steps are similar to corresponding steps of FIGS. **29-30** and will not be described again in detail. As before, pattern classifiers are preferably not trained under certain conditions. Beginning at step **1300** of FIG. **33**, the training system determines whether the test subject is asleep (or is otherwise inactive) and, if so, begins receiving atrial and ventricular IEGM signals sensed within the test subject and identifying individual events therein, at step **1302**, for the purposes of training one or more pattern classifiers. At step **1304**, the training system identifies a current rhythm type within the test subject. That is, the training system determines whether the heart is currently undergoing predominantly AR, AV, PR or PV rhythms, which is then identified as the "current" rhythm type. In one example, the training system tracks the latest one-minute epoch of data and identifies the predominant rhythm within that one-minute epoch. The training system selects a particular pattern classifier for training based on the current rhythm type. In other words, in this example, four separate pattern classifiers are provided, one for each of the four main rhythm

types. An AR pattern classifier is activated for training if the current predominant rhythm is AR. A PR classifier is activated for training if the current predominant rhythm is PR; etc. Alternatively, a single pattern classifier is used, which is loaded with different classifier parameters depending upon the rhythm type.

At steps **1306** and **1308**, the training system extracts morphological parameters and interval-based parameters for use in training the selected pattern classifier. At step **1310**, the current respiration status of the test subject is identified (normal or abnormal) using, e.g., an external system. At step **1312**, the training system then trains the selected pattern classifier to discriminate patients with normal respiration from patients with abnormal respiration while also identifying the optimal morphological parameters and interval-based parameters for use with the current rhythm type. For example, while training the AR pattern classifier, the training system might determine that tPDI and ffPDI are the most useful morphological parameters when discriminating normal and abnormal respiration during AR cardiac rhythms. While training the AV pattern classifier, the training system might instead determine that aPDI and fftPDI are the most useful morphological parameters for use in discriminating normal from abnormal respiration during AV cardiac rhythms. As such, these parameters can then be specifically selected for use with the different pattern classifiers when the pattern classifiers are activated for use in actually detecting abnormal respiration. Once a sufficient amount of data has been processed from the particular test subject, another test subject is selected. A new test subject may be selected, at step **1313**. Training continues until a sufficient amount of data from a sufficient number of test subjects has been processed so that the pattern classifier(s) can reliably discriminate normal and abnormal respiration.

FIG. **34** illustrates the use of the pattern classifier(s) trained within FIG. **33**. That is, FIG. **34** illustrates steps performed by a pacer/ICD that has been implanted within a patient and which includes one or more trained pattern classifiers. Beginning at step **1314**, the pacer/ICD determines whether the patient is asleep (if needed) and, if so, proceeds to detect abnormal respiration. (Preferably, abnormal respiration detection is not performed under conditions that were excluded during training, such as during AF/AT.) Assuming abnormal respiration is to be detected, step **1316** is then performed wherein the pacer/ICD senses IEGM signals and identifies individual events therein. At step **1318**, the pacer/ICD identifies the current rhythm type of the patient (i.e. the predominant rhythm type over an epoch of interest) and activates the corresponding pattern classifier. For example, if AR is the current cardiac rhythm type (i.e. the predominant rhythm type over the latest one-minute epoch), then the pattern classifier specifically trained for use with AR data is activated. Conversely, if AV is the current cardiac rhythm type, then the pattern classifier specifically trained for use with AV data is activated. At step **1320**, the pacer/ICD extracts the particular morphological parameters identified during step **1312** of FIG. **33** as being optimal for use with the current rhythm type. At step **1322**, the pacer/ICD extracts the particular interval-based parameters identified during step **1312** of FIG. **33** as being optimal for use with the current rhythm type. At step **1324**, the pacer/ICD then detects abnormal respiration by applying the extracted parameters to the particular pattern classifier that has been activated. In this manner, during AR rhythm, an AR pattern classifier is used to detect abnormal respiration based on parameters previously deemed to be optimal for use with AR. During AV rhythm, an AV pattern classifier is used to detect abnormal respiration based on parameters previously deemed to be optimal for use with AV; etc. Again, the pattern classifier preferably detects whether the patient is subject to abnormal respiration but does not necessarily detect individual episode of abnormal respiration. As already, explained, the pattern classifier can instead be trained to identify individual episodes of abnormal respiration. The severity of abnormal respiration within the patient may then be determined at step **1326** and appropriate therapy/warnings delivered, if warranted.

Although the training techniques described herein employ an external training system, training may instead be performed within the pacer/ICD, if so equipped. In other words, the pacer/ICD may be provided with a pattern classifier not yet trained (or only partially trained). Following device implant, the pacer/ICD then trains its pattern classifier using IEGM signals sensed by the pacer/ICD along with signals from another (non-pattern recognition-based) apnea detector. Examples of non-pattern recognition-based apnea detectors are described in U.S. patent application Ser. Nos. 10/883,857 and 10/821,241 cited above.

The various techniques of FIGS. **28-34** may be implemented within any appropriate implantable medical device. The techniques are preferably performed substantially in real-time to promptly detect episodes of abnormal respiration. However, the techniques may instead be applied to stored IEGM data to detect episodes of abnormal respiration that have already occurred. Moreover, principles of the invention are also applicable to external devices when used in conjunction with implanted devices. For example, an external programmer device may be equipped to detect abnormal respiration within a patient based on IEGM data sensed by a device implanted within the patient and sent via telemetry to the programmer for processing.

For the sake of completeness, an exemplary pacer/ICD employing components for implementing the techniques of FIGS. **28-34** is illustrated in FIG. **35**. Most of the components of the pacer/ICD of FIG. **35** are the same as that of FIG. **17** and will not be re-described. Only pertinent differences will be discussed. Pacer/ICD **1400** of FIG. **34** includes a microcontroller **1460**, which incorporates a cardiac rhythm-type determination unit **1402** operative to determine a current cardiac rhythm type of the patient; a cardiac cycle detection unit **1404** operative to identify cardiac cycles within the electrical signals; a morphological parameter detection unit **1406** operative to detect one or more morphological parameters associated with the cardiac cycles; an interval-based parameter detection unit **1408** operative to detect one or more interval-based parameters associated with the cardiac cycles; a pattern classifier **1412** trained to discriminate, at least, between normal and abnormal respiration based on the parameters associated with the cardiac cycles; and an abnormal respiration detector **1410** operative to detect abnormal respiration by applying the parameters of the cardiac cycles to the pattern classifier **1412**. These microcontroller components may be provided in addition to the various microcontroller components shown in FIG. **17**, which are not repeated within FIG. **35**. Some of these components (particularly the pattern classifier) may alternatively be implemented within external programmer **702** and/or bedside monitor **22** for discriminating normal respiration from abnormal respiration within the patient based on data detected within the patient and transmitted via telemetry circuit **700**.

What have been described are various systems and methods for tracking respiration, detecting episodes of abnormal respiration and delivering therapy in response thereto using an implantable system controlled by a pacer or ICD. However, principles of the invention may be exploiting using other

implantable systems or in accordance with other techniques. Thus, while the invention has been described with reference to particular exemplary embodiments, modifications can be made thereto without departing from the scope of the invention.

What is claimed is:

1. A method for detecting abnormal respiration using an implantable medical device, the method comprising:

sensing cardiac electrical signals within a patient in which the device is implanted;

determining a cardiac rhythm type of the patient;

identifying cardiac cycles within the electrical signals;

detecting one or more parameters associated with the cardiac cycles and as a function of the cardiac rhythm type; and

detecting abnormal respiration by applying the parameters of the cardiac cycles to a device trained to discriminate between normal and abnormal respiration for the cardiac rhythm type.

2. The method of claim **1** wherein detecting abnormal respiration by applying the parameters of the cardiac cycles to the trained device is performed to discriminate between normal respiration and apneic/hypopneic respiration.

3. The method of claim **1** wherein detecting abnormal respiration by applying the parameters of the cardiac cycles to the trained device is performed to discriminate among normal respiration, obstructive apneic/hypopneic respiration and central apneic/hypopneic respiration.

4. The method of claim **1** wherein detecting one or more parameters includes detecting interval-based parameters associated with the cardiac cycles.

5. The method of claim **4** wherein the interval-based parameters include one or more of R-R, P-R, P-P and QT intervals.

6. The method of claim **1** wherein the morphological parameters include one or more of vPPI, tPDI, aPDI, ffPDI, and fftPDI.

7. The method of claim **1** wherein detecting parameters associated with the cardiac cycles includes extracting time-domain features from the parameters, the time-domain features being applied to the trained device.

8. The method of claim **7** wherein the time-domain features include mean and standard deviations of the parameters.

9. The method of claim **1** wherein detecting parameters associated with the cardiac cycles includes frequency features from the parameters, the frequency-domain features being applied to the trained device.

10. The method of claim **1** wherein detecting abnormal respiration by applying the parameters of the cardiac cycles to the trained device further includes evaluating a severity of abnormal respiration.

11. The method of claim **1** wherein detecting abnormal respiration by applying the parameters of the cardiac cycles to the trained device is performed by applying only those parameters detected within a particular epoch of time.

12. The method of claim **1** further including detecting whether the patient is asleep and wherein detecting abnormal respiration by applying the parameters of the cardiac cycles to the trained device is performed only using parameters detected while the patient is asleep.

13. The method of claim **1** wherein the implantable device is equipped to perform one or more of bi-ventricular and bi-atrial sensing and wherein detecting abnormal respiration is performed by applying parameters derived from cardiac cycles extracted from one or more of bi-ventricular and bi-atrial cardiac signals to the device trained to discriminate between normal and abnormal respiration.

14. The method of claim **1** wherein detecting abnormal respiration by applying the parameters of the cardiac cycles to the trained device is performed to discriminate between patients with substantially normal respiration and patients subject to abnormal respiration.

15. The method of claim **1** wherein detecting abnormal respiration by applying the parameters of the cardiac cycles to the trained device is performed to detect individual episodes of abnormal respiration.

16. A system for detecting abnormal respiration using an implantable medical device having a device trained to discriminating between normal and abnormal respiration, the system comprising:

means for sensing cardiac electrical signals within a patient in which the device is implanted;

means for determining a cardiac rhythm type;

means for identifying cardiac cycles within the electrical signals;

means for detecting one or more parameters associated with the cardiac cycles and as a function of the cardiac rhythm type;

means for discriminating between normal and abnormal respiration using the parameters of the cardiac cycles.

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